ROLE OF CHOROIDAL THICKNESS AND PSYCHOLOGICAL STRESS IN CENTRAL SEROUS CHORIORETINOPATHY: A CROSS-SECTIONAL STUDY

DISSERTATION SUBMITTED TOWARDS FULFILLMENT OF THE RULES AND REGULATIONS FOR THE M.S. BRANCH III OPHTHALMOLOGY EXAMINATION OF THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY TO BE HELD IN MAY, 2020

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SUBMITTED BY
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BONA FIDE CERTIFICATE

This is to certify that this dissertation entitled "**Role of choroidal thickness and psychological stress in Central serous chorioretinopathy: a cross-sectional study**" done towards fulfillment of the requirements of the Tamil Nadu Dr MGR Medical University, Chennai for MS Branch III Ophthalmology examination to be conducted in May 2020, is the bona fide original work of Dr. Reshmi Mathews, Post Graduate student in Ophthalmology, Christian Medical College, Vellore.

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DECLARATION

I hereby declare that this dissertation entitled "**Role of choroidal thickness and psychological stress in Central serous chorioretinopathy: a cross-sectional study**" done towards fulfillment of the requirements of the Tamil Nadu Dr MGR Medical University, Chennai for MS Branch III Ophthalmology examination to be conducted in May 2020, comprises my original research work, and information taken from secondary sources has received due acknowledgement and citation.

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INTRODUCTION

Central serous chorioretinopathy (CSCR) is a chorioretinal disorder with systemic associations and multifactorial etiology. It is characterized by serous detachment of the neurosensory retina, which is usually located at the posterior pole.(1) Patients with CSCR present with relative central scotoma, metamorphopsia, micropsia, dyschromatopsia and blurring of vision.(2) Fundus examination shows a well-demarcated, oval-shaped area of neurosensory retinal detachment at the posterior pole.(1) The disease is usually self-limiting, and resolves spontaneously in most of the patients within a period of about three months, without significant visual loss.(3) However, many patients develop recurrence, or develop chronic disease, leading to RPE atrophy and pigmentation in the macular area, with varying degrees of visual loss.(4)

The disease was first described by Albrect von Graefe as ‘central retinitis’ in 1866. Over the years, there have been numerous attempts to study the pathogenesis of CSCR. With the advent of investigative tools like Fundus Fluorescein Angiography (FFA), Indocyanine Green Angiography (ICGA), and Optic Coherence Tomography (OCT), we now have a better understanding of the pathogenesis of the disease.

Changes noted in the choroidal vasculature in patients with CSCR, using these techniques, have led to the concept that CSCR is primarily a disease of the choroidal vasculature.(5) FFA has demonstrated leakage of fluid from focal areas of retinal pigment epithelial breaks in patients with CSCR.(6) ICGA has demonstrated choroidal hyper perfusion in patients with CSCR.(7)

Further, newer Optical Coherence Tomography systems (Enhanced depth imaging spectral-domain OCT – EDI-OCT, and Swept-Source OCT – SS-OCT) demonstrated the thickening of the choroid in patients with CSCR, supporting the involvement of the choroid in CSCR.(8) Choroidal vascular hyperpermeability leads to increased tissue hydrostatic pressure beneath the retinal pigment epithelium. Under normal conditions, there is a balance between the oncotic and tissue hydrostatic pressure, due to which fluid is pumped from the retina towards the choroid. When this balance is disrupted and hydrostatic pressure increases, fluid flows in the reverse direction, from the choroid to the retina, which results in disruption and 'micro-rips' in the retinal pigment epithelium, and accumulation of sub retinal fluid that results in CSCR.(9)

Studies conducted in different parts of the world, using newer Optical Coherence Tomography systems, have found that choroidal thickness is significantly increased in eyes with CSCR.(10–14) CSCR belongs to the Pachychoroid spectrum of diseases.(15) This spectrum includes three other diseases, which are also associated with a thick choroid, namely Pachychoroid pigment epitheliopathy, Pachychoroid neovasculopathy and Polypoidal choroidal vasculopathy.(16)

CSCR is influenced by exogenous and endogenous (systemic) factors that cause alterations in choroidal vasculature. Steroids, both exogenous and endogenous, have also been implicated in CSCR. Steroids are thought to cause an increase in choroidal vascular permeability.(17) They inhibit collagen synthesis and cause capillary wall fragility and hyper permeability, resulting in fluid leakage into the subretinal space.(18) In addition to this, steroids are also known to cause hypertension, which is considered to be an independent risk factor for CSCR (19). Endogenous

hypercortisolism, seen in Cushing syndrome, ACTH secreting pituitary tumors, ectopic ACTH secreting tumors, or adrenal tumors,(20) has been associated with increased incidence of CSCR.

Several studies have shown the association of psychological stress and Type A personality with CSCR.(21)(22) Stress and Type A personality are associated with endogenous hypercortisolism.(23) Stress activates the hypothalamic-pituitary-adrenal axis, causing increased secretion of cortisol.(24) Psychological stress has been well-proven to be associated with the development of CSCR, in various studies done in different parts of the world.(21,25–28)

Although both choroidal thickness and psychological stress have been studied in patients with CSCR, the correlation between these two factors has not been studied so far. The aim of our study was to study the role of choroidal thickness and psychological stress in patients with Central serous chorioretinopathy.

AIM AND OBJECTIVES

Aim :

To evaluate the role of choroidal thickness and psychological stress in patients with Central serous chorioretinopathy (CSCR)

Objectives:

1. To compare the subfoveal choroidal thickness of the involved eye in patients with unilateral Central serous chorioretinopathy - CSCR (Group 1), with that of the uninvolved fellow eye, and with that of age and gender-matched controls without CSCR (Group 2)
2. To compare the stress scores of patients with CSCR (Group 1) with those of the control group (Group 2)
3. To study the correlation between the subfoveal choroidal thickness and stress scores of the study subjects

REVIEW OF LITERATURE

Central serous chorioretinopathy (CSCR) is a disease, which has been extensively studied since 1866, when it was first described by von Graefe. The advent of newer modalities of investigations has improved our knowledge regarding the etiology and pathogenesis of the disease.

CSCR was known by several names since its first description in 1866, as our understanding of the disease entity has also evolved over the years. Von Graefe named it as Recurrent central retinitis in 1866. In 1922, Horniker described it as capillaro-spastic central retinitis because of his belief that vasospasm was the pathophysiology behind the disease.(29) The advent of Fundus Fluorescein Angiography (FFA) revolutionized our understanding of the disease, and Maumenee described CSCR as a disease in which the choroid and retinal pigment epithelium (RPE) were the main tissues involved.(30) Further, Gass coined the term, Central Serous Chorio retinopathy(CSCR), based on his studies with FFA, which proved the involvement of the RPE and the choroid.(2) Since then, the term, Central Serous Chorioretinopathy(CSCR) has been widely accepted, and has been in use.

Central serous chorioretinopathy is characterized by serous detachment of the retina at the posterior pole, usually at the macula.(1) It is the fourth most common form of non-surgical retinopathy after age-related macular degeneration, diabetic retinopathy and retinal vein occlusions.(1)

Patients with CSCR present with relative central scotoma, metamorphopsia, micropsia, dyschromatopsia and blurring of vision.(2) Refraction in such patients may show a hypermetropic shift. Fundus examination reveals a well-demarcated, oval-shaped area of neurosensory retinal detachment, usually at the posterior pole.(3)

Natural history of CSCR

The disease is usually self-limiting, and resolves spontaneously within a period of three to four months, with a good visual prognosis. Visual recovery is dependent on the initial visual acuity at presentation. Better the vision at the time of presentation, better the final visual recovery, with best outcomes associated with presenting vision of 6/9 or more.(31) Following the resolution of CSCR, there can be areas of RPE atrophy or pigmentary changes at the macula, which generally do not progress, and the visual outcome is usually good.(32) In the absence of any intervention, 15 to 50% of cases of CSCR are associated with recurrence.(33) Recurrence is associated with poorer visual outcome, decreased stereopsis and color vision.(1) Five percentage of the cases progress to chronic form of CSCR, which is characterized by widespread diffuse RPE abnormality, RPE atrophy amounting to geographic atrophy, shallow persistent serous detachments and pigment clumps at the macula.(34) Patients are generally older with a poorer visual outcome.

Sequalae of CSCR

Sequalae are usually found in chronic CSCR persisting beyond a period of four months, and are usually associated with poorer visual prognosis.(1) These include:(35)

1. RPE depigmentation
2. Geographic atrophy

3. Subretinal fibrinous deposits
4. Choroidal neovascular membrane (CNVM)
5. Attenuation of the neurosensory retina, mainly photoreceptor layer

Presence of CNVM, recurrent CSCR, persistent subretinal fluid and persistent pigment epithelial detachment (PED) have been found to be associated with poor final visual acuity.(36) Duration of symptoms more than five years, posterior cystoid retinal degeneration and foveal atrophy are other factors resulting in poor visual outcomes in CSCR.(37–39)

Epidemiology

There is limited data regarding the incidence of CSCR. In a population-based study done by Kitzmann et al. in Minnesota, USA, the incidence of CSCR was reported to be 5.8 per 100,000, with a higher incidence in males (63.6 %), and a mean age at diagnosis of 41 years.(40) Another population-based study by Tsai et al. in Taiwan, reported an annual incidence of 0.21%, with a higher incidence in males (0.27 %) than in females (0.15 %), and peak age of incidence at 35 -39 years.(41) In a retrospective study by Sahoo et al. from India, the prevalence of CSCR was estimated to be 1.7% with an 88% male preponderance and peak incidence between 35 to 45 years.(42) However, CSCR has also been reported below 20 years, as well as above 60 years.(34,43) At the time of diagnosis, CSCR is mostly unilateral, but can eventually involve both eyes.(44) Bilateral and multifocal CSCR is found more in Asian population as compared to Caucasians or African Americans.(45)

Anatomy of the retina

The retina is the innermost layer of the eyeball. It is comprised of the following ten layers, from outer to inner –(46)

1. Retinal pigment epithelium (RPE)
2. Photoreceptor layer (layer of rods and cones)
3. External limiting membrane
4. Outer nuclear layer
5. Outer plexiform layer
6. Inner nuclear layer
7. Inner plexiform layer
8. Ganglion cell layer
9. Nerve fibre layer
10. Internal limiting membrane

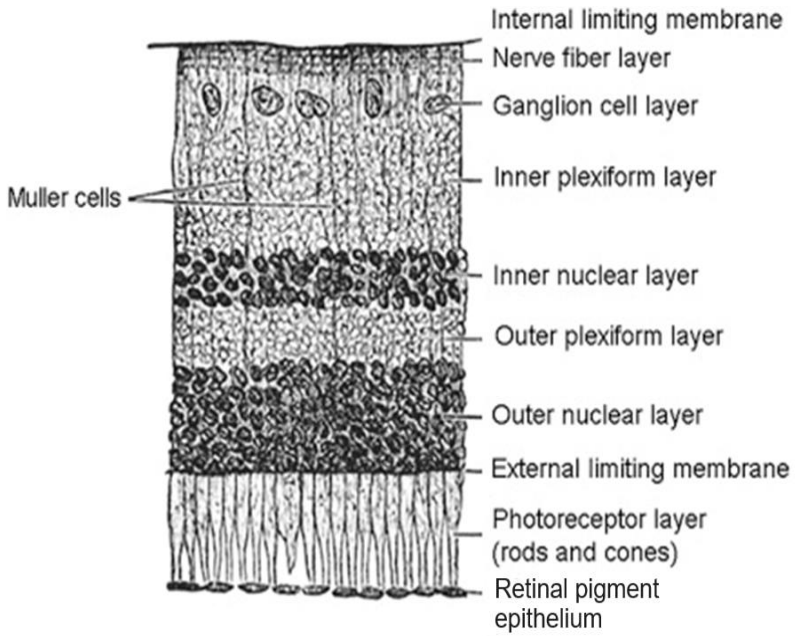


Figure 1: Layers of the retina

The inner retinal layers receive their blood supply from the branches of the central retinal artery, whereas the outer retina is nourished by the choroidal circulation.(46) The neurosensory retina consists of all the layers excluding the retinal pigment epithelium. In central serous chorioretinopathy (CSCR), there is accumulation of subretinal fluid (SRF) between the retinal pigment epithelium (RPE) and the neurosensory retina.

Anatomy of the choroid

The choroid consists of five layers (from outer to inner)-(47)

1. Supra choroidal lamina (Lamina fusca)
2. Haller's layer (large vessel layer)
3. Sattler's layer (medium-sized vessel layer)

4. Layer of choriocapillaris
5. Bruch's membrane

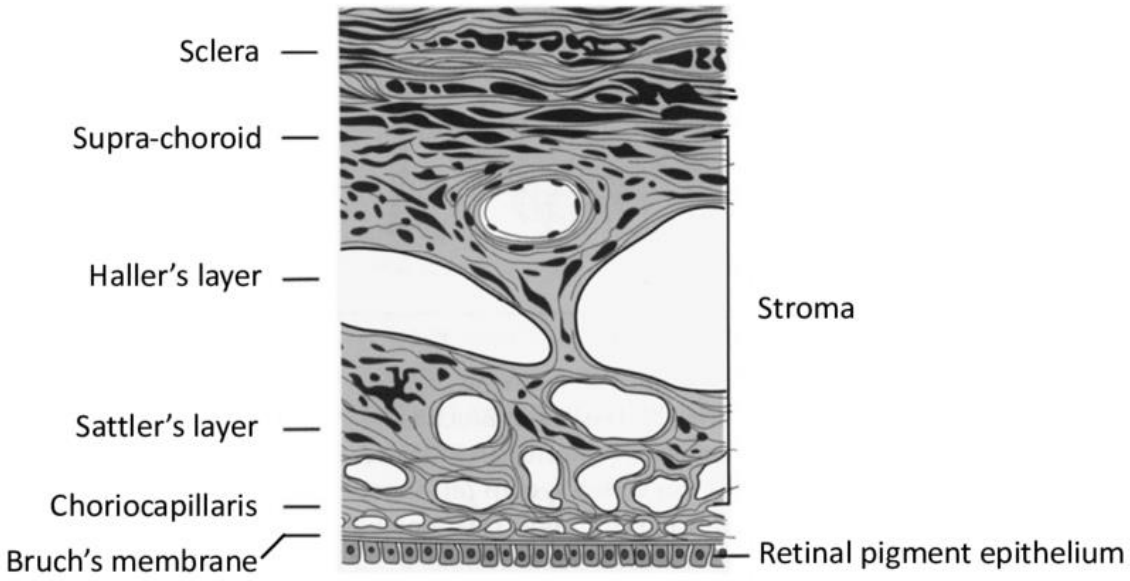


Figure 2: Layers of the choroid

Pathophysiology of CSCR

Over the years, there have been numerous attempts to study the pathogenesis of CSCR. The exact mechanism still remains unclear, but with the advent of investigative tools like Fundus Fluorescein Angiography (FFA), Indocyanine Green Angiography (ICGA), and Optical Coherence Tomography (OCT), researchers have been able to study and characterize the disease better.

Role of the Retinal Pigment Epithelium (RPE)

Role of the retinal pigment epithelium in CSCR is not very well understood. Various theories have been put forward. Fundus autofluorescence (FAF) has demonstrated areas

of RPE breech and corresponding areas of leak. The most widely accepted theory is that the increased hydrostatic pressure within the choroid hampers the barrier function of the RPE, resulting in areas of 'micro -rips' or 'blow- out.' Pigment epithelial detachments found in CSCR also point toward RPE decompensation as a result of raised choroidal hydrostatic pressures.(9) However, Negi and Marmor, in a study done on rabbits, proved that there is flow of fluid from the sub retinal space into the choroid from an area of RPE loss, rather from the choroid into the sub retinal space.(48) An alternate theory states that, it is the loss of polarity of the RPE cells that results in active pumping of the fluid into the subretinal space.(49)

OCT imaging of the RPE in CSCR has successfully demonstrated focal areas of RPE breaks and corresponding areas of leak on FFA.(50) Another OCT-based study of the RPE demonstrated RPE abnormalities also in the uninvolved eyes of CSCR patients.(51)

Role of the choroid

Changes noted in the choroid and choroidal vasculature in patients with CSCR, in recent years, have led to the concept that CSCR is primarily a disease of the choroidal vasculature.(5) ICGA has demonstrated choroidal hyperperfusion in patients with CSCR.(7) Further, with the advent of newer Optical Coherence Tomography systems (Enhanced depth imaging spectral-domain OCT – EDI-OCT, and Swept-Source OCT – SS-OCT), thickening of the choroid in patients with CSCR has been noted, supporting the involvement of the choroid in CSCR.(52)

Basic principles of Optical Coherence Tomography(OCT)

Optical Coherence Tomography (OCT) is a non-invasive, non-contact modality of imaging, which produces cross sectional images of intra ocular tissues. The invention of OCT has revolutionized human understanding of a whole spectrum of retinal diseases.

OCT utilizes light in the near infra-red spectrum, which is much faster than sound waves. Low-coherence interferometry is the underlying principle of OCT.(53) An interferometer splits light from a source, into two separate paths, one to the reference mirror and the second to the sample. It also combines the light travelling back from the two paths at the output, where interference takes place. Superimposition of coherent waves takes place and their electromagnetic field amplitudes add constructively (i.e. they reinforce each other), or destructively (i.e. they cancel each other out), or meet at any condition in between. The output is measured as an electrical signal using a photo detector.

There are two main OCT technologies –

1. Time Domain (TD-OCT)
2. Fourier Domain (FD-OCT)

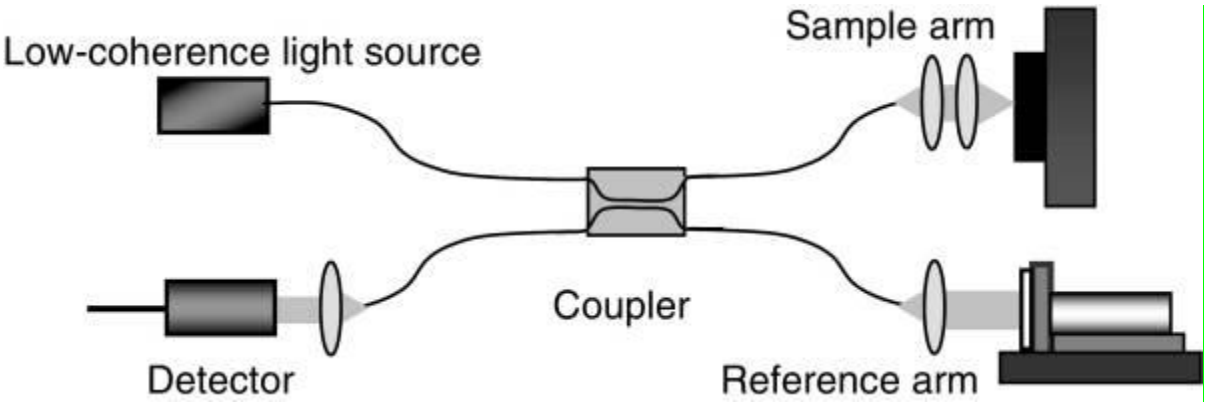


Figure 3: Schematic representation of the principle of Optical Coherence Tomography

Time domain (TD-OCT)

In a time domain OCT, for a given position of the reference mirror, a corresponding interference pattern is formed only with light that travelled the same distance through the sample arm, including the depth of the tissue being imaged.(54) Thus, the distance of the mirror is altered along the direction of light corresponding to the interference pattern from the backscattered light from the corresponding depths within the sample. In other words, the reference mirror in a TD-OCT is moving.

Fourier domain (FD-OCT)

In FD-OCT, the light echoes come at the same time from all axial depths, and are detected as changes in the source spectrum, with all the spectral components captured simultaneously. The main difference of FD- OCT from TD- OCT is that the reference arm in an FD-OCT has a stationary mirror instead of a moving one as in TD-OCT.(54) This makes the FD-OCT systems capable of higher data acquisition speeds. The current generated in an FD-OCT detection system by incoming light is a function dependent on the source wavelength (or the wavenumber)

sampled at that instant. The acquired wavenumber-dependent data are transformed into axial scan information by performing an inverse Fourier transform.

There are two types of Fourier domain OCT –

- Spectral Domain OCT (SD-OCT)
- Swept Source OCT (SS-OCT)

Spectral Domain OCT (SD-OCT):

SD-OCT is similar to TD-OCT, but the point detector is replaced by a spectrometer after the two returning beams recombine.(54) The spectrometer uses a diffraction grating to spatially separate out the different wavelengths into a line image, which is recorded by a high speed line scan camera.

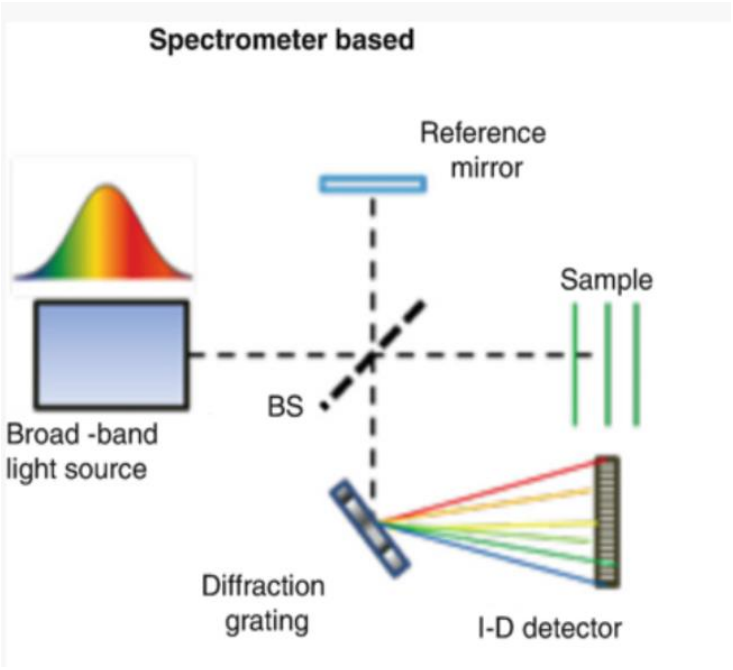


Figure 4: Principle of Spectral Domain OCT

Swept Source OCT (SS-OCT)

Principle:

The optical setup in SS-OCT is similar to TD-OCT, but instead of a broadband light source, an optical source is used, which rapidly sweeps a narrow line-width over a wide range of wavelengths.(53) During one sweep, each wavelength of the interferometric signal is detected sequentially by a high speed photo-detector. The reference beam is reflected from a fixed mirror. The interference pattern with the light backscattered from the sample is detected by a point detector. Point detection is an advantage that SS-OCT has over SD-OCT because it has a greater signal-to-noise ratio as compared to area or line detectors. Because of the way the source laser is scanned across the available broadband in SS-OCT, the output is a wavenumber-dependent photo-current that is recorded by the point detector simultaneously with the scanning of the narrow-band laser. The quantity of interest, the depth profile or A-scan, is also obtained by performing the Fourier-transform of the detected signal over one sweep of the laser across the available broadband. Since the light from a swept-source consists of a laser signal with a continuously changing wavelength over time, the coherence length of the scanned laser determines the maximum imaging depth of the system, while the wavelength range over which the laser is swept determines the axial resolution of the system. Therefore, a scanning laser with a narrow linewidth enables a deeper probing depth while a wider sweep range produces OCT images with higher axial resolution.

These newer technologies in OCT imaging have helped us to visualize the retinal and choroidal layers and identify the pathophysiology in a much better way.

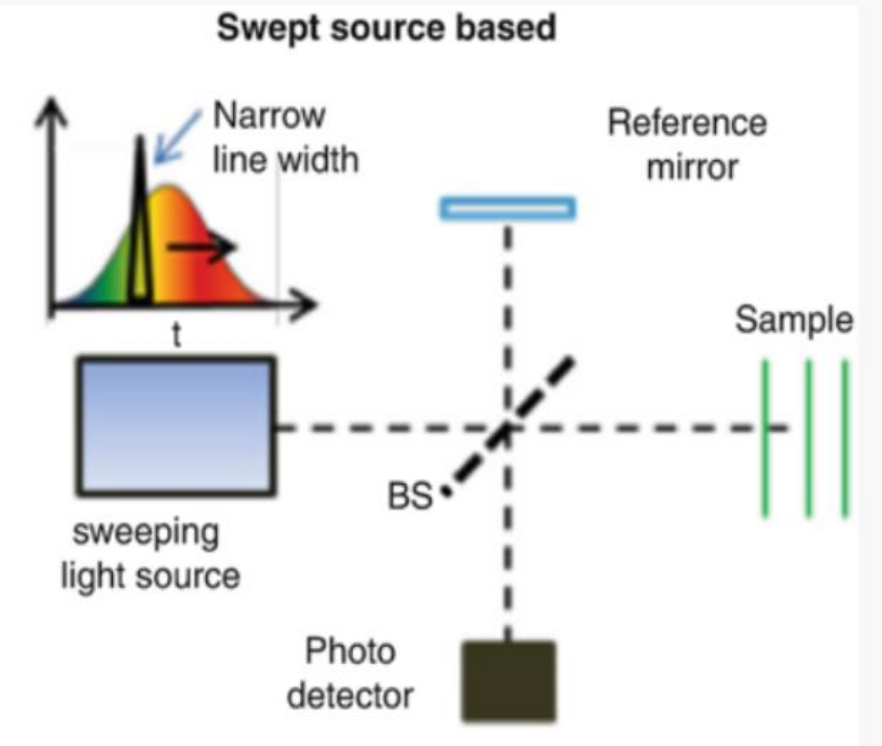


Figure 5: Principle of Swept Source OCT

A standard nomenclature system was developed in 2013 by an international panel with expertise in retinal imaging (International Nomenclature for Optical Coherence Tomography [IN-OCT] Panel) to define a consensus for OCT imaging terminology.(55) The panel consisted of a group of retina specialists, who then unanimously named each layer on the OCT, and this has been followed as standard.

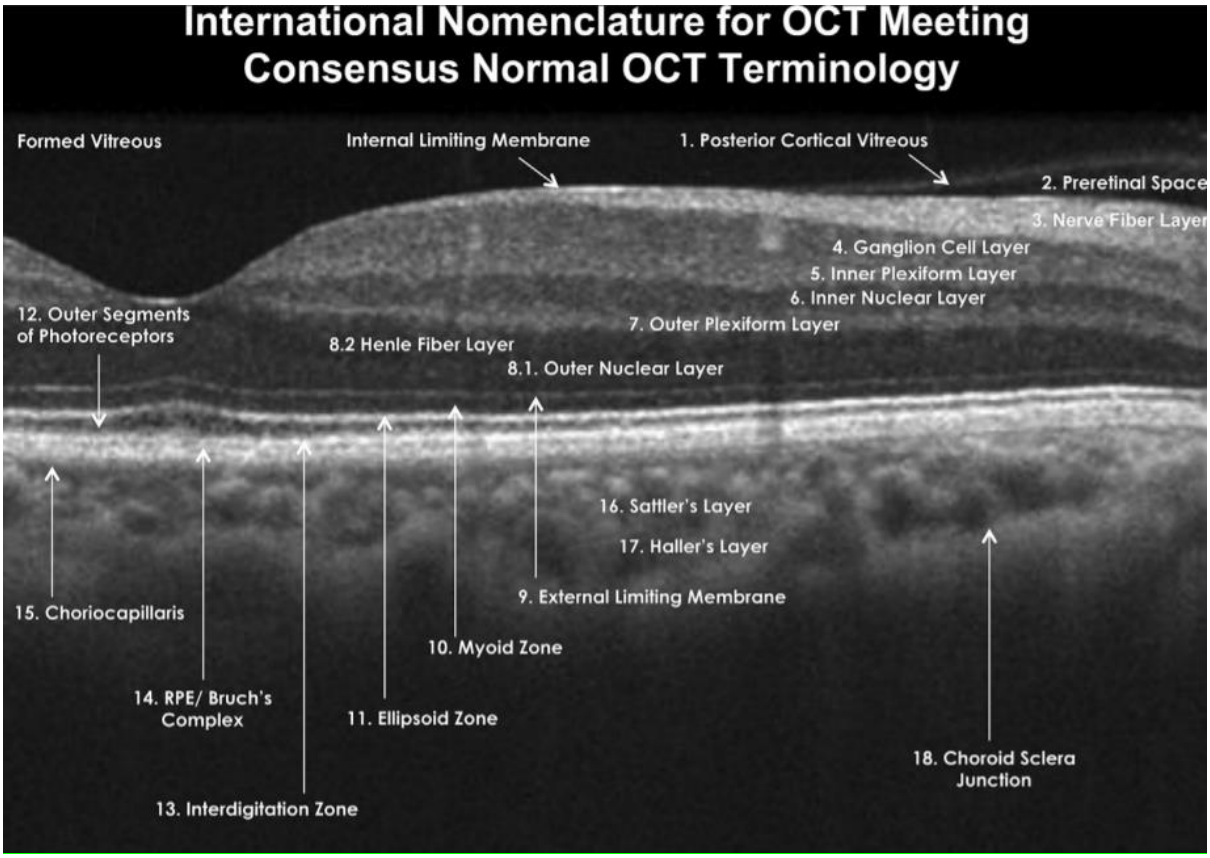


Figure 6: IN-OCT panel nomenclature-Normal OCT terminology

Using advanced OCT imaging techniques, numerous studies have been carried out in different parts of the world to establish the normative data regarding the normal choroidal thickness and the various factors affecting the choroidal thickness. Majority of the studies have looked at subfoveal choroidal thickness (SFCT).

Ikuno et al., in their study done in Japan, using SS-OCT, found the mean choroidal thickness to be 354 ± 111 μm at the fovea, 364 ± 86 μm superiorly, 345 ± 108 μm inferiorly, 227 ± 532 μm nasally, and 337 ± 102 μm temporally.(52) Another study using SS-OCT, done in Spain by Abadia et al., comparing the subfoveal choroidal thickness in healthy individuals and patients with Type 2 Diabetes mellitus, demonstrated a mean SFCT of 228.1±78.8 μm in healthy controls

and 183.5±72.9 μm in diabetic patients with DME.(56) There was a recent study from India by Bhayana et al. in 2017, using SS-OCT, which aimed to establish normative data of choroidal thickness in healthy Indian population in the age group of 19 to 60 years. The mean SFCT in this study was 299.10 ± 131.2 μm.(57)

Prior to the advent of SS-OCT, there have been a number of studies, which have looked at the choroidal thickness using Spectral Domain OCT (SD-OCT), and have obtained similar results. A study done by Manjunath et al., using Cirrus HD-OCT (SD-OCT) on 34 healthy individuals, found a mean SFCT of 272 +/- 81 μm.(58) In the study by Kong et al., the mean SFCT of 724 normal healthy eyes of 374 study subjects, measured by EDI-OCT, was 292.6 ± 94μm.(59) A mean SFCT of 287 +/- 76 μm was reported in a study by Spaide et al., conducted on 30 healthy individuals, using EDI OCT.(60)

There have also been studies comparing the choroidal thickness measured using Enhanced depth imaging Spectral domain OCT and Swept source OCT. In a cross-sectional study of 82 healthy eyes of 46 patients, by Copete et al., the mean SFCT was found to be 279.4±96.9 μm (range, 84–506μm) with SD-OCT and 285.7±88.9 μm (range 130–527μm) with SS-OCT.(61) Yet another study done in India, by Narendran et al., on 62 normal eyes of 31 healthy individuals, arrived at the conclusion that the subfoveal choroidal thickness was comparable between SS-OCT and SD-OCT images**,** and that the differences between the two increased in eyes with thicker choroid.(62)

Choroidal thickness is affected by a number of factors.

- **Age:** According to Ding et al., in patients younger than 60 years, there was no correlation of SFCT with age. However, in patients older than 60 years, there was a negative correlation, with a decline in SFCT by 5.4 μm for every one year of life.(63) In the study done by Margolis et al., SFCT decreased by 15.6 μm per decade of life irrespective of age.(60) Another study done by Ikuno et al., also arrived at a similar conclusion, stating that SFCT decreased by 14 μm per decade, irrespective of age.(64) According to the Beijing Eye Study, which was a large population-based cross-sectional study involving 3468 participants, the SFCT decreased by 4.1 μm for each year of increase in age.(65) However, the participants of the study were between the age group of 50 to 93 years with a mean of 64.6+/- 9.8 years.
- **Gender:** Gender has also been found to have a role in the thickness of the choroid, with male gender found to have thicker choroids as compared to their age-matched female counterparts. A cross- sectional study done on 93 eyes of 93 healthy volunteers by Li et al., concluded that the subfoveal choroidal thickness was 62 μm thicker in men than in women, adjusted for age and axial length.(66) According to the Beijing Eye Study also, SFCT was thicker in the male population (P<.001).(65) Another study by Zeng et al. on 620 eyes of 310 healthy volunteers found the mean SFCT to be significantly higher in males (298.02 ± 101.47) μm as compared to females (256.28 ± 90.87) μm (P< .05).(67)
- **Axial length:** Increase in axial length causes a decrease in choroidal thickness. In the study by Li et al., every 1 mm increase in axial length decreased the SFCT by

58.2μm.(66) However, according to the Beijing Eye study, SFCT decreased by 32 μm for every 1 mm increase in axial length.(65)

- **Refractive error:** Myopic refractive error is associated with choroidal thinning. The Beijing Eye Study demonstrated a mean decrease in SFCT of 15μm for every dioptre of myopia.(65) Another study by Ikuno et al., on 86 eyes of 43 healthy subjects, found 9.3 μm of thinning in SFCT for every dioptre of myopia.(52)
- **Diurnal variation:** Subfoveal choroidal thickness is found to be highest in the early morning, followed by a progressive decrease toward the evening hours.(68,69) A study by Usui et al., on 38 eyes of 19 healthy volunteers, found the SFCT to be thickest between 3 and 9 am, and thinnest between 3 and 9 pm.(68) In the study by Tan et al. on 12 healthy volunteers, the highest mean choroidal thickness was found to be 372.2 μm at 9:00 AM, with a progressive decrease to 340.6 μm at 5:00 PM.(69) Both the studies attributed the diurnal variation in choroidal thickness to alterations in the systolic blood pressure.
- **Blood pressure:** Changes in blood pressure affect choroidal thickness.(70) The study done by Kim et al. on 12 eyes of six patients with malignant hypertension, found an increase in choroidal thickness, which decreased with control of blood pressure.(70) However, another study by Akay et al., comparing the choroidal thickness of 80 hypertensive patients and 80 healthy controls demonstrated thinner choroids among hypertensives.(71) This result was attributed to arteriolar stenosis and vascular contraction due to raised blood pressure in the choroidal vasculature.
- **Diabetes:** Several investigators have found a thinner choroid in patients with diabetic retinopathy. A study by Ambiya et al. on 100 eyes of diabetic patients without diabetic

retinopathy, 100 eyes with various stages of diabetic retinopathy, and 100 eyes of healthy patients without diabetes, found that SFCT decreased with increasing duration of diabetes.(72) The decrease in SFCT was significant after the onset of severe diabetic retinopathy. They also concluded that the decrease is proportionate to the severity of diabetic retinopathy. Another study by Sudhalkar et al. on 227 eyes of 125 subjects with diabetes and 197 eyes of 110 age-matched healthy subjects arrived at a similar conclusion. In their study also, the SFCT in eyes of diabetic patients was found to be thinner as compared to the eyes of age-matched healthy subjects without diabetes.(73) They also found that the SFCT in patients with diabetes, but without diabetic retinopathy was thicker compared to that in subjects with diabetic retinopathy. The involvement of the choroid can be attributed to the microvascular changes within the choroidal vasculature, which in turn, can compromise the blood supply to the outer retinal layers, leading to some of the manifestations of diabetic retinopathy.

- **Pregnancy:** The effect of pregnancy on choroidal thickness has also been studied. It has been shown that pregnancy is associated with an increase in the choroidal thickness.(74) Pregnancy is known to produce a state of high cardiac output, which in turn increases the heart rate, cardiac contractility and circulating volume.(75) Thus, the blood flow to all the organs, including the choroid, is increased.
- **Smoking:** Chronic smoking has been associated with decrease in choroidal thickness.(76) Nicotine impairs nitric oxide-mediated vaso-dilation, which affects choroidal blood flow.(77)

- **Alcohol**: Alcohol has been proposed to cause an increase in the choroidal thickness through an acetyl choline-mediated vasodilation of the choroidal vessels. Acetyl choline is produced in the liver during the metabolism of alcohol (ethanol).(78) A study done by Kang et al. on 30 subjects, demonstrated an increase in the mean SFCT during the first 60 minutes, followed by a decrease during the next 120 minutes after ethanol consumption.(79) Alcohol activates the sympathetic nervous system and brings about vaso constriction through the norepinephrine pathway.(80) Chronic alcohol use also impairs the endothelial nitric oxide mediated vaso dilation, hampering the choroidal blood flow.(81)

Pachychoroid disease spectrum

A "pachychoroid" (pachy- thick) is defined as an abnormal and permanent increase in choroidal thickness, often showing dilated choroidal vessels and other structural alterations of the normal choroidal architecture.(16) It has also been described in terms of an enlarged Haller's layer, which compresses the vessels of the inner choroid, and is best visualized using newer OCT systems.(82)

The following are the common characteristics of the pachychoroid spectrum:(83)

- Thickening of the choroid
- Thinning of the choriocapillaris and the Sattler's layer
- Dilated veins in the Haller's layer

The term "pachychoroid" can be used for a subfoveal choroidal thickness of >390 μm.(15)

CSCR is a part of the pachychoroid spectrum. Other entities that belong to this spectrum are:

1. Pachychoroid Pigment Epitheliopathy (PPE)
2. Pachychoroid Neo Vasculopathy (PNV)
3. Polypoidal Choroidal Vasculopathy (PCV)

Longstanding increase in the choroidal thickness results in chronic choroidal congestion and secondary backpressure changes, resulting in damage to the retinal pigment epithelium (RPE) and Bruch's membrane.(29) Choroidal vascular hyperpermeability leads to increased tissue hydrostatic pressure beneath the retinal pigment epithelium. When this balance is disrupted and hydrostatic pressure increases, fluid flows in the reverse direction, from the choroid to the retina, which results in disruption and 'micro-rips' in the retinal pigment epithelium, and accumulation of subretinal fluid that results in CSCR.(9)

Hyperpermeable choroid is thought to play a pivotal role in the pathogenesis of CSCR. Stasis, ischemia or inflammation result in a hyperpermeable choroid.(84) The staining of the inner choroid seen during mid-phase of ICG angiography provides evidence for the same.(85,86) Further, a thickened choroid has been demonstrated in CSCR, using imaging modalities like SS-OCT and EDI-OCT, thus substantiating the pivotal role of the pachychoroid in CSCR. pivotal role of the pachychoroid in CSCR.

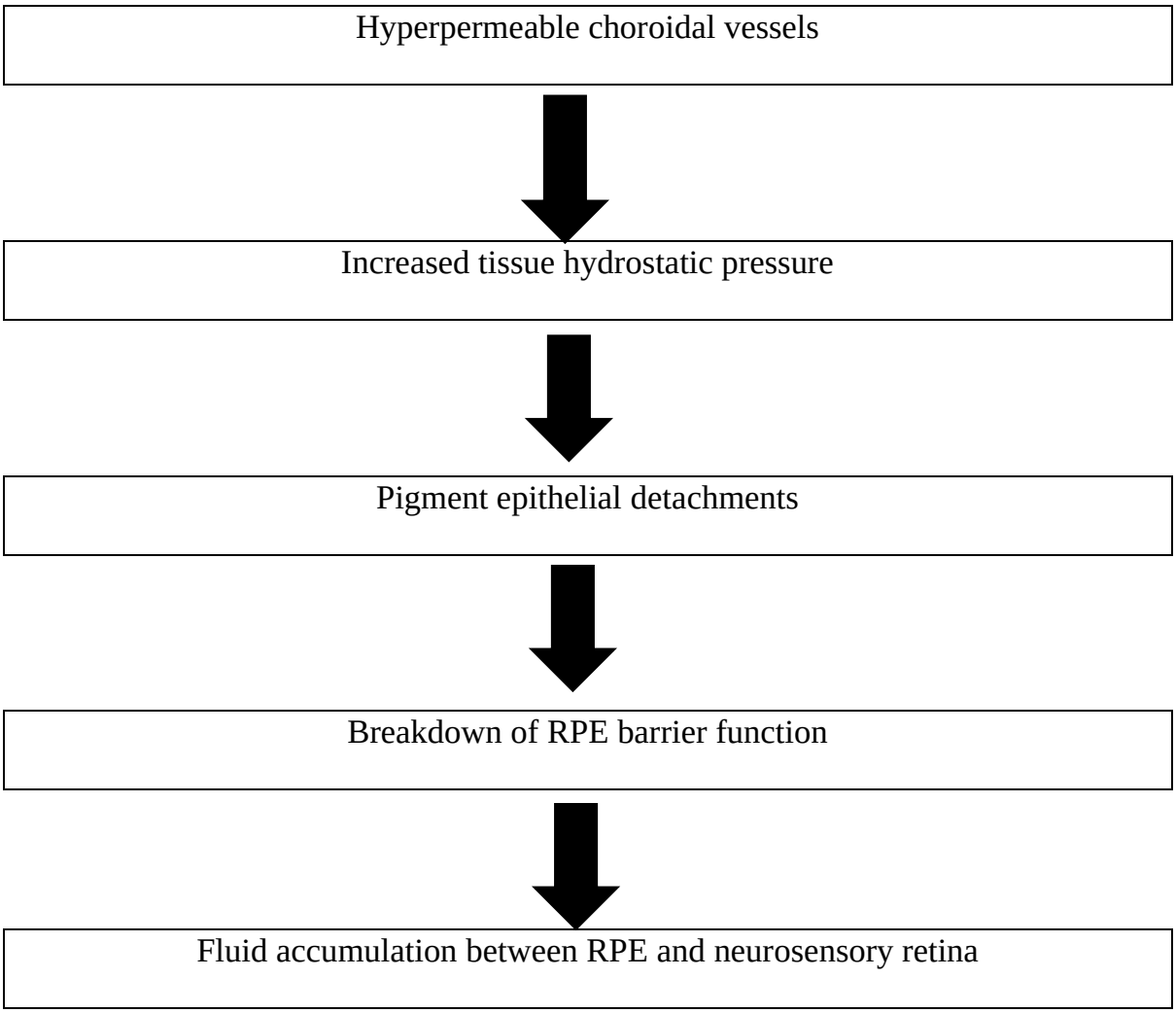


Figure 7: Pathogenesis of CSCR

The newer and advanced modalities of retinal imaging have enabled us to accurately measure the choroidal thickness in CSCR. Numerous studies all over the world have extensively studied the involvement of the choroid in CSCR, and have successfully demonstrated a relatively thicker choroid in patients with the disease.

Kuroda et al., in their study conducted in Japan, on 35 eyes of 27 subjects with CSCR and 35 healthy age-matched control eyes, found that the subfoveal choroidal thickness in all eyes with

CSCR was significantly greater than that of the control eyes (*P* <.01).(8) In this study, the mean subfoveal choroidal thickness in CSCR eyes was 475 ± 138 μm and 372 ± 120 μm in control eyes.(69) Another study done in Japan by Maruko et al. showed that the mean subfoveal choroidal thickness in 66 patients with unilateral CSCR was significantly higher than that in the fellow eyes (414 ± 109 μm vs. 350 ± 116 μm)(*P*< .001). Brandl et al. conducted a study on ten CSCR eyes with age and gender-matched controls, and showed that the sub foveal choroidal thickness in CSCR eyes (421.0 μm±72.2μm) was much higher than that of the eyes of normal controls (282.28 μm±29.73μm).(10) In fellow eyes, the average subfoveal choroidal thickness at baseline was 308.1 μm±67.2μm.They also demonstrated that at the three-month follow up, although the choroidal thickness reduced in association with the resolution of CSCR, the choroidal thickness never reached the normal state. A study done by Kim et al. on 30 patients with CSCR and 30 age-matched normal controls, comparing the SFCT in affected eyes, unaffected fellow eyes and normal eyes of controls demonstrated increased choroidal thickness in the affected eyes (*P*<.001).(87) The mean SFCT of the CSCR affected eyes, unaffected fellow eyes, and normal control eyes were 445.58±100.25, 378.35±117.44, and 266.80±55.45 μm, respectively. This study further demonstrated that the unaffected fellow eyes also have a thicker choroid as compared to normal controls(*P*<.001). In a meta-analysis by Chen et al. on 1108 eyes (397 CSCR eyes, 228 unaffected fellow eyes and 483 eyes of normal controls), the mean SFCT of the affected eyes, unaffected fellow eyes, and normal control eyes was 413.1 ± 93.0 μm, 337.9 ± 90.9 μm, 277.6 ± 73.4 μm, respectively.(88) This study also established a significant increase in SFCT, not only in clinically affected eyes with CSCR*(P*<.00001), but also in clinically unaffected fellow eyes(*P*<.00001). There has been one published study on this subject from

India by Arora et al. This study included 112 normal eyes, 84 eyes with acute, treatment naïve CSCR and 69 fellow eyes. Choroidal thickness was measured using NIDEK SD-OCT. The mean SFCT of CSCR eyes, fellow eyes and normal eyes was 429 ± 74.18 μm, 360 ± 57.99 μm and 301.80 ± 46.59 μm ($P < .001$).(13)

Fundus Fluorescein Angiography(FFA) in CSCR

FFA is used to identify the foci of leakage in CSCR, which is a prerequisite for planning treatment with laser or Photo Dynamic Therapy (PDT), if required. Areas of leak show up as pin point areas of hyperflourescence, which intensify during the late phases. Classically, two patterns of leak are described in FFA in acute CSCR-(1)

- Ink blot pattern
- Smoke stack pattern

In ink blot pattern, the leak starts as a central point of hyperflourescence, which progressively increases circumferentially. In smoke stack pattern, the hyperfluorescence ascends slightly upwards and laterally, giving rise to a mushroom-like area of hyperflourescence.(1) Ink blot pattern is more common than the smoke stack pattern. The study by Turchetti et al. on 455 eyes with CSCR, found that 88.81% of the patients had an ink blot pattern of leakage in FFA, and the remaining 11.19% had a smoke stack pattern.(89) How et al., in their study on 128 CSCR eyes of Asian patients also found the ink blot leakage pattern to be the most common, found in 103 patients (80%), followed by the smoke stack pattern, found in 20 patients (16%); four patients had both patterns.(45) Macula was the most common site of leakage in their study (76%), followed by peripapillary area, and then periphery. 56% of their study patients had a unifocal

leak, and 44% had multifocal leak. Mishra et al. studied 542 eyes of 376 patients with acute CSCR, and found multifocal leaks in more than half of their study population (55.72%), and unifocal leak in the rest (44.28%).(90) Again, ink blot pattern was the most common (75.65%) in their study. They observed that the commonest site of leakage was at the macula (69.37%), followed by periphery (20.30%), and then the peripapillary area (7.80%). The remaining (2.58%) eyes had leakage at more than one site. In another study by Laishram et al. on 50 patients, 72% patients were found to have an ink blot pattern of leak.(91)

In cases of chronic CSCR, diffuse as well as patchy areas of hyperfluorescence (window defects) due to RPE atrophy are seen.(1) Pigment epithelial detachments (PED) are also seen on FFA and OCT in patients with CSCR. In a study by Quereshi et al. on 104 eyes with CSCR, PED was seen in 63% study subjects.(92) The combination the RPE dysfunction and choroidal vascular hyperpermeability seen in CSCR along with the increased hydrostatic pressure in the choroid results in PED. Further, the breakdown of the RPE causes accumulation of subretinal fluid resulting in CSCR.(29)

Indocyanine Green Angiography (ICGA) in CSCR

ICGA demonstrates the choroidal vasculature much better as compared to FFA. Hence, it is very useful in CSCR as a guide to Photo Dynamic Therapy(PDT). Indocyanine, the dye used In ICGA, is twice the molecular weight of fluorescein, and it stains the vascular walls, intravascular contents and the extravascular structures like the choroidal stroma.(93) The ICG spectrum is also better transmitted through the RPE, thus providing an additional advantage for imaging of the choroid.(94)

In CSCR, in the early phases of ICGA, there is a delay in filling of the choriocapillaris, showing up as hypofluorescent areas.(95) Dilation of large choroidal veins along with large areas of hyperfluorescence with blurred margins, seen during the mid-phase of ICGA, persisting through the late phases, is suggestive of choroidal vascular hyperpermeability.(96)

Factors implicated in the etiopathogenesis of CSCR

Age and gender

Male gender has been considered to be a risk factor for CSCR.(40–42) In a population-based study done by Kitzmann et al, incidence in males (63.6%) was higher than females, and the mean age at diagnosis was 41 years.(40) Tsai et al. also demonstrated a male preponderance in their study with a peak age of incidence at 35 -39 years.(41) In the study by Sahoo et al. from India, an 88% male preponderance was reported with a peak incidence between 35 to 45 years.(42) Although the exact mechanism is not clear, it is postulated to be due to a testosterone-mediated pathway.(97) High levels of testosterone have been implicated as a risk factor for CSCR, and androgen receptors have been discovered in the human retinal pigment epithelial cells.(98) The peak age of incidence of CSCR is between 35-45 years.(42) Older age groups are considered to be less prone to develop CSCR due to decreasing levels of testosterone with advancing age.(99)

Hypertension

Hypertension has been postulated as a risk factor for CSCR.(100,101) In the study by Haimovici et al. on 312 CSCR cases and 312 CSCR controls, untreated hypertension was identified as a risk factor for CSCR (P = .01).(102) Tittl et al. also arrived at similar conclusion in their study on 230 CSCR cases and 230 controls (P = .008).(103) In a study done by Venkatesh et al. on 32

CSCR patients and 32 healthy controls, the mean systolic blood pressure was 123.56+/- 4.8 mm Hg in the CSCR group and 113.63+/ -12.62 mm Hg in the control group (*P*= .02).(104) Mean diastolic blood pressure was 84.75+/- 10.2 mm Hg in the CSCR group and 76.75+/ -0.4 mm Hg in the control group (*P*= .007).(100)

Untreated hypertension leads to arteriosclerotic changes with constriction of vessels in the choroidal circulation. Chronically elevated blood pressures severely affect the choroidal vessels and cause fibrinoid necrosis of the choroidal arterioles and their occlusion, leading to breakdown of the outer blood retinal barrier. These alterations facilitate the leakage of fluid into the sub-RPE space, and may result in the development of CSCR.(102)

Diabetes mellitus

The role of Diabetes mellitus has also been studied in relation to CSCR. Diabetes is thought to cause a thinner choroid.(72,73) Similar to its effect on other blood vessels in the human body, diabetes causes microvascular changes within the choroidal vasculature, thus compromising the blood supply to the choroid. However, its role in the subfoveal choroidal thickness in CSCR has been debatable, and the outcome of various studies have been conflicting. The study by Chatziralli et al. on 183 CSCR patients and 183 age and gender-matched controls, showed that diabetes was not a significant risk factor for CSCR(*P* = .63).(104) However, another study done by Haimvoci et al. on 312 CSCR patients and 312 controls, found an association of diabetes mellitus with CSCR (*P*< .0001) on multivariate analysis.(102)

Substance abuse

Substance abuse, like smoking and alcohol abuse, has been implicated as a risk factor for CSCR. Smoking and alcohol abuse are behavioral coping adaptations to psychological stress.(105) Both nicotine and alcohol have been proposed to impair nitric oxide-mediated vaso-dilation, which affects choroidal blood flow.(77,106) In addition, alcohol and nicotine also induce vasoconstriction through norepinephrine-mediated pathway.(107) Haimovici et al. showed alcohol ($P< .001$) and tobacco use ($P= .003$) to be risk factors for CSCR in their study.(102)

Pregnancy

Pregnancy is a risk factor for CSCR, with resolution of the disease in the post partum period.(101,108) This is attributed to the neuroendocrine and hemodynamic changes in pregnancy.(109) Pregnancy is also known to be a state of hyper cortisolism.(110) Haimovici et al. showed pregnancy to be a risk factor for CSCR in their study ($P< .003$).(102) There have been various case reports of visual impairment in pregnancy associated with CSCR.(108,111)

Helicobacter pylori infection

Another interesting association of CSCR is with gastric Helicobacter pylori, which is a gram negative bacterium that causes chronic infections of the gastro intestinal tract, leading to peptic ulcer disease and dyspepsia(112,113). The possible mechanism is postulated to be a molecular mimicry between the bacterial cell wall antigen and the homologous proteins on the endothelium of the choroidal vessels.(113)

In a retrospective observational study by Cotticelli et al. on 23 CSCR patients and 23 controls, the prevalence of H. pylori infection was 78.2% in CSCR group and 43.5% in

control subjects (P<0.03).(114) Roshani et al. also proved H. pylori infection to be a significant risk factor for CSCR (P< .001).(112)

Obstructive sleep apnea (OSA)

Obstructive sleep apnea is thought to be associated with higher risk for the development of CSCR, although the exact pathophysiological mechanism has not been fully understood. It has been stated by Kloos et al. that OSA increases the sympathetic activity, which in turn, increases cortisol levels and results in CSCR.(115) The study done by Chatziralli et al. on 183 CSCR patients and 183 age and gender-matched controls, brought out an association between the two (P =.010).(104) However, another study by Brodie et al. on 48 CSCR patients and 48 age and gender-matched controls failed to prove an association between CSCR and OSA (P=1.000).(116)

Reactive airway disease

The relationship of CSCR with reactive airway disease has been attributed to the chronic use of steroids in these patients.(117) The results of different studies on this subject have been conflicting. Tittle et al. found no association between asthma and CSCR in their study.(118) Haimovici et al. could not find an association between CSCR and reactive airway disease in their study by univariate analysis; however, on stepwise logistic regression, they were able to establish such an association.(102)

Cardiovascular disease

The relationship between CSCR and cardiovascular disease has been controversial. CSCR and cardiovascular disease share some possible common predisposing factors, including imbalance between coagulation, coagulysis and personality A-type.(119,120) However, in the study by

Chatziralli et al., no significant association between coronary artery disease and CSCR was found on multivariate analysis (*P*= .097).

Role of steroids

Steroids, both exogenous and endogenous, have been implicated in the pathogenesis of CSCR by the various mechanisms listed below:

- Steroids may directly increase choroidal hyperpermeability.(17)
- Steroids inhibit collagen synthesis and cause capillary wall fragility and hyperpermeability. This, in turn, causes decompensation of the choroidal circulation and fluid leakage into the subretinal space.(18)
- Glucocorticoids have also been shown to cause blood coagulation, leading to choroidal hypoperfusion.(121)
- In addition to this, steroids are also known to cause hypertension, which is considered to be an independent risk factor for CSCR.(122)
- Glucocorticoids can also activate the mineralocorticoid pathway. In the human body, cortisol binds to Mineralocorticoid receptors (MR) as well, due to their structural similarity to the Glucocorticoid Receptors (GR). Mineralocorticoids cause salt and water retention in the intravascular compartment, leading to hypertension. Mineralocorticoid Receptors (MR) are also present in the choroidal vessels.(123)
- In the human body, glucocorticoids are secreted by the adrenal glands. The production of endogenous glucocorticoids is regulated by Adrenocorticotropic Hormone (ACTH) secreted by the pituitary gland, which is further regulated by Corticotropin-releasing

Hormone (CRH) secreted by the hypothalamus.(124) Endogenous hypercortisolism, seen in Cushing syndrome, ACTH secreting pituitary tumours, ectopic ACTH secreting tumours, or adrenal tumours,(124) has been associated with increased incidence of CSCR. Any form of stress increases the hypothalamic secretion of CRH, which increases ACTH secretion, and in turn, increases the secretion of glucocorticoids.(24)

Collagen vascular diseases

The association of these diseases with CSCR has been studied, but the results have been inconsistent, and the exact mechanism is still unclear. Some studies have documented an association of CSCR with auto immune diseases like collagen vascular diseases through a steroid mediated mechanism.(102,104)

Post organ transplantation

CSCR has been reported in patients after organ transplantation like, kidney, bone marrow and liver transplantation. Patients who develop CSCR after organ transplantation are thought to do so because of the long term corticosteroid use.(125)

Medication

Several medications have been implicated in the etiopathogenesis of CSCR. These include psycho pharmacological medications, anti histaminics, antacids, anti-reflux medications, phosphodiesterase-5 inhibitors and sympathomimetics.(102,126) Psychopharmacological medications like anxiolytic agents and antidepressants are used in the treatment of anxiety, depression and stress-related disorders, which are known risk factors for CSCR. Anti histaminics are used for the treatment of allergic airway disease, and antacids and anti-reflux medications in

the treatment of acid peptic disease, which are again risk factors for CSCR. Phosphodiesterase-5 inhibitors like Sildenafil are used in the treatment of erectile dysfunction, and they have been found to cause an engorgement of choroidal vessels.(127)

Stress and CSCR

The association of psychological stress with CSCR has been well proven.(21) Stress and Type A personality are associated with endogenous hypercortisolism.(22) Stress activates the hypothalamic-pituitary-adrenal axis, causing increased secretion of cortisol.(24,128)

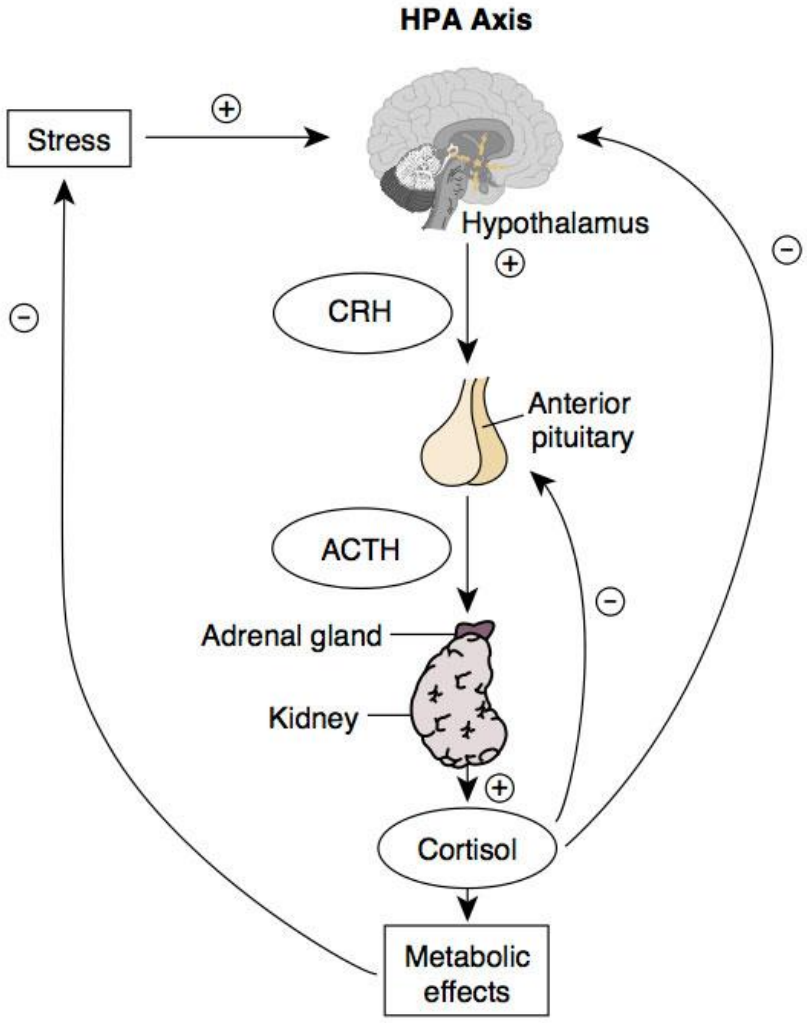


Figure 8: The hypothalamic-pituitary-adrenal (HPA) axis

The association of psychological stress with the development of CSCR has been extensively studied by investigators from different parts of the world.(21,22,25,26,129–131) Various studies have found the stress scores to be significantly elevated in CSCR patients as compared to the normal population. In a study by Agarwal et al. in India, including 54 CSCR patients and 54 controls, the stress scores in the CSCR group were found to be elevated.(*P*= .042)(21) They used the National Stress Awareness Day Stress Questionnaire, published by the International stress management association, UK, to assess the stress scores in their study subjects. In another study by Bazzazi et al. in Iran, on 30 CSCR patients and 30 controls, the stress scores in the CSCR group were found to be significantly elevated as compared to the control group (*P*= .000), using the Hamilton Anxiety Rating Scale (HAM-A).(25) Another study done in Turkey by Sahin et al., on 30 cases with CSCR and 30 controls, showed a lower quality of life and more psychological problems in cases as compared to the control group.(131) A study by Puri et al. in India, including 30 CSCR and 30 controls, further showed higher stress levels in the CSCR group.(130) They used the Holmes Rahe Scale in their study. They pointed out that individuals staying away from family, nearing retirement, going through a change of profession, change in working conditions or changes in sleep pattern had considerably higher stress levels, possibly predisposing them to developing CSCR. Rouvass et al., in their hospital-based study conducted in Greece, observed a higher incidence of CSCR during the time of economic crisis (2005 -2012).(28) They implied that the emotional stimuli and the stress brought about by the financial crisis had lead to the drastic increase in the incidence of CSCR. Green et al., in their hospital-based study conducted over a one-year period (1986-87), observed 55 cases of CSCR

among the US Airforce aviators during this period.(132) Therefore, CSCR may be associated with high stress job profiles. Conrad et al., in their study on 35 CSCR patients, found inadequate coping mechanisms in these patients, which were postulated to predispose them to developing CSCR.(129) Gelbert et al. studied 33 patients with CSCR, and demonstrated the occurrence of a disturbing psychological event prior to the onset of symptoms.(26) Type A personality is a strong risk factor for CSCR by a similar mechanism, due to constant activation of the neuro endocrine system, resulting in increased levels of cortisol and epinephrine in the blood as compared to Type B personality.(22,133)

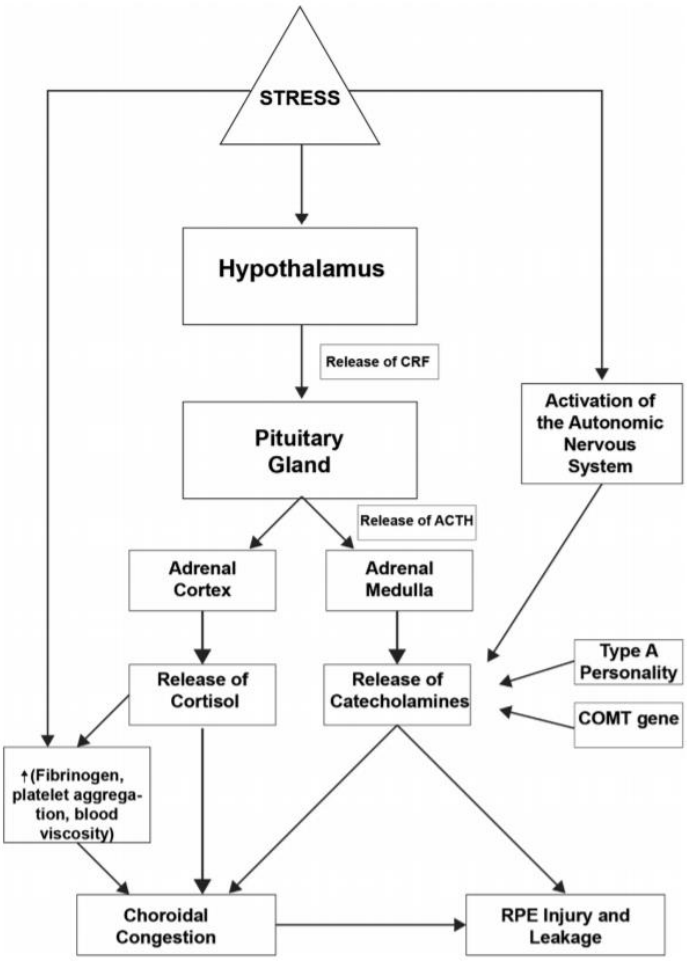


Figure 9: Role of stress in CSCR(148)

Shift duty and sleep disturbance

CSCR is closely associated with sleep disturbances. Various studies have found lack of sleep and shift work to be risk factors for CSCR.(134,135) Sleep disturbances are associated with increased activity of the hypothalamic-pituitary-adrenal axis and the autonomic sympatho-adrenal pathway, resulting in increased secretion of cortisol and catecholamine hormones.(136) Therefore, both cortisol and catecholamine levels are dysregulated in shift workers and those with sleep disturbances, predisposing them to developing CSCR.(135) Recently, the role of melatonin has been explored as a protective factor for CSCR. Melatonin is secreted by the pineal gland, following a circadian rhythm with peak secretion at night during sleep.(137) The secretion of melatonin is hampered in shift workers by exposure to light during night hours.(138) With this background, the role of oral melatonin in the treatment of non-resolving CSCR has been studied with promising results.(139)

Family history

CSCR is thought to be associated with genetic predisposition. In a study including 27 patients with CSCR and 80 of their relatives, mostly siblings, positive fundus findings were found in 35 relatives (44%).(140) In another study by Lehmann et al. on 16 first and second degree relatives of five CSCR patients, 50% of the relatives were found to have a thicker choroid, suggesting that pachychoroid could be an inherited condition, which predisposes to CSCR.(15)

Treatment of CSCR

Acute CSCR has a self-resolving natural course, with excellent visual prognosis. Management of an acute episode of CSCR involves careful observation and modification of risk factors. Therefore, a detailed history is of paramount importance in bringing out any of the risk factors leading to CSCR. Dealing with the identified factors is the first step in the management of CSCR. Careful observation without any active intervention is usually done for three to four months, anticipating spontaneous resolution of the subretinal fluid.(3) OCT scans have to be repeated at every follow-up to compare the level of subretinal fluid with that in the baseline scan. Decrease in the height of the subretinal fluid indicates spontaneously closed leakage, and such cases can be observed for more time.(3)

Risk factor modification: This is essential during the period of observation. Corticosteroid use is a modifiable risk factor. History should be elicited to bring out the use of steroid in any form - systemic (oral or intravenous) or local (e.g. skin creams, nasal sprays, joint injections).(29) The drug should be discontinued or tapered, in consultation with a physician. Steroid sparing agents can be considered for the treatment of the systemic illness in such patients.

Psychological stress and Type A personality have been associated with CSCR. After identifying such a patient, effective stress management should be advised. Anxiolytic medication can be given in the initial days.(3) Other modifiable risk factors like substance abuse and use of drugs like phosphodiesterase-5 inhibitors should also be addressed.

Conventional laser photocoagulation: This is used for an extrafoveal leak to hasten SRF resolution. The focal laser injury causes recruitment of healthy RPE cells as response, or stimulates RPE pumping function near the treated area, thus clearing out the subretinal

fluid.(141) Various studies have demonstrated a faster resolution of SRF in eyes treated with focal laser.(142) However, there is a risk of the laser burn resulting in permanent damage to the RPE, which could lead to a scotoma or the subsequent formation of a choroidal neovascular membrane (CNVM).

Micro pulse diode laser photocoagulation: This uses subthreshold diode laser energy to a point source leakage. In this technique, the damage to the RPE is minimized, and there is no clinically visible laser-induced damage.(143) A study done by Verma et al., comparing the efficacy of conventional argon laser photocoagulation with Micro pulse diode laser, demonstrated a similar resolution of SRF at 12 weeks follow up. However, reduction in contrast sensitivity and scotomas were more in the conventional argon laser group.(144)

Photodynamic therapy (PDT): PDT with verteporfin has been used to treat CSCR. PDT works by inducing choroidal hypoperfusion, and vascular remodeling to negate choroidal hyperpermeability, which is the main pathophysiology in CSCR.(145) In order to minimize the risk of choroidal ischemia, RPE atrophy, RPE rip and choroidal neovascular membrane (CNVM), certain safety measures like low-fluence PDT (25 J/cm^2) and half-dose verteporfin PDT (3 mg/m^2) were introduced, which have now been widely used with good results.(146,147)

Medical management: Spironolactone and eplerenone are aldosterone antagonist agents with additional anti-androgen properties, with promising results in the treatment of CSCR.(148) In the study by Herold et al., in which 21 patients with non-resolving CSCR were treated with spironolactone, the long term benefits in terms of recurrence, final visual acuity and reduction in subretinal fluid were promising.(149) They had followed up the study subjects up to 12 months. However, in the study by Cakir et al. on 24 patients with non-resolving CSCR, 29% had a

complete resolution of sub retinal fluid, 33% had a transient reduction and 25 % failed to respond. Treatment had to be stopped in 13% patients due to adverse effects of Eplerenone.(150) Melatonin has been recently tried in the treatment of long standing CSCR, and the results have been found to be promising. There was improvement in visual acuity and reduction in the central macular thickness in patients treated with Melatonin.(139) However, long term follow up studies regarding the drug are not available. In the study by Gramajo et al. on 13 patients with chronic CSCR, who were treated with Melatonin for one month, it was observed that there was a significant improvement in BCVA ($P < .05$) and decrease in central macular thickness ($P < .01$). However, one patient had a recurrence during one year follow up.(139)

Ketoconazole, an antifungal agent, has been tried in the medical management of CSCR due to its anti-glucocorticoid effect.(151) Ketoconazole blocks the conversion of cholesterol to androgenic glucocorticoid end products. However, Meyerle et al. could not prove a significant therapeutic benefit in terms of improved visual acuity or decrease in the height of the CSCR on OCT, despite the decrease in the endogenous cortisol levels.(152) Aspirin has been postulated to be effective in treating CSCR due to its fibrinolytic and anti-platelet action.(153) Other pharmacological agents tried in the management of CSCR include rifampicin, methotrexate and adrenergic antagonists, with varying results.

Although acute CSCR is self-limiting and resolves within three to four months, the disease may go on to chronicity and develop sequelae with visual loss. Therefore, appropriate identification of risk factors and adequate management of the disease is important.

MATERIALS AND METHODS

Study design

This was a hospital-based, cross sectional study

Setting

This study was conducted in the Department of Ophthalmology, Christian Medical College, Vellore. Christian Medical College, Vellore is a tertiary care teaching center in South India. The average number of patients seen per week in the outpatient clinics of the Department of Ophthalmology, Christian Medical College, Vellore, is 2500-2800.

Duration of the study

The study was conducted over a period of twenty months, from February 2018 to September 2019,after receiving the approval of the Institutional Review Board (IRB Min. No. 11094, dated 10.01.2018).

Patient selection

The study included patients with Central Serous Chorioretinopathy (CSCR), seen in the outpatient clinics of the Department of Ophthalmology (Group 1), and age & gender-matched patients without Central Serous Chorioretinopathy (Group 2). Patients fulfilling the eligibility criteria of the study were enrolled, after obtaining informed consent.

Inclusion criteria

Group 1: Patients with unilateral CSCR, who were seen in the Ophthalmology OPD

Group 2: Age and gender-matched patients without CSCR, who were seen in the Ophthalmology OPD, randomly selected (1:2 ratio – for every patient with CSCR in Group 1, two age and gender-matched patients without CSCR in Group 2)

Method of random selection of controls (Group 2)

The selection of controls (Group 2), from the list of new registrations for OPD patients for the day, was based on a random start using a pseudo random number, generated using a calculator. The number equivalent to the last two digits from the right, of the pseudo random number generated, was chosen. Every patient in the list, starting with the random start, was considered, and the first patient who fulfilled the appropriate age and gender matching criteria, was recruited into the study. The age of each control (Group 2) was matched to within 2.5 years above or below that of the corresponding case (Group 1).

Exclusion criteria

1. Duration of CSCR-related symptoms more than four months
2. Patients who have had any intervention for the disease
3. Age less than 20 years, and more than 60 years
4. Patients on steroid medication
5. Post organ transplant patients
6. Pregnant women
7. Patients with history/ clinical features of endogenous hypercortisolism
8. Patients with any other retinal/ choroidal/ optic disc pathology, which may interfere with diagnosis of CSCR, and/ or may be associated with changes in SFCT (list appended - Appendix 5)

9. Patients with history of ocular trauma/ surgery/ intravitreal injections/ laser procedures

10. Myopia or hyperopia of more than 2 dioptres, or a difference of more than 1 dioptre between the two eyes of the patient

11. Axial length of less than 21.5 mm or more than 24.5 mm, or a difference of more than 0.5 mm between the two eyes of the patient

12. Patients with media opacity that interferes with clear OCT image acquisition

Informed consent and recruitment:

The information sheet explaining the study was given to all patients. Information sheets were available in English, Hindi and Tamil. For illiterate participants, the information sheet was read out in the language understood by them. Patients were then recruited into the study after obtaining their informed consent.

Methodology

All the participants of the study had a complete ophthalmological examination, including refraction (by autorefractometry), slit lamp bio microscopy, applanation tonometry and dilated fundus examination, as part of the routine evaluation of all patients in the outpatient clinics of the Department of Ophthalmology.

Figure 10: Clinical examination

Patients with CSCR (Group 1) also had an OCT scan of the macula (Swept source OCT) and fundus fluorescein angiography, as part of the routine management of CSCR. OCT scan of the macula was also done in patients in Group 2. OCT scan was done between 11 AM to 2 PM for all the study patients in order to minimize the effect of diurnal variation of choroidal thickness.

In addition, axial length measurement was done by Optical Biometry, and measurement of blood pressure was done in all patients in the study.

Subfoveal choroidal thickness (SFCT) of both eyes of all the participants was measured using a standard protocol. One horizontal and one vertical 6 mm line scan of the macula of each eye of all study participants was done. SFCT was measured at the fovea, from the outer part of the hyper reflective line corresponding to the base of the retinal pigment epithelial layer to the hypo reflective line or margin corresponding to the sclero choroidal interface.(154) Three consecutive readings of SFCT in each scan were taken, and the mean of the six readings of SFCT in each eye was taken as the final reading of SFCT. The subretinal fluid height in eyes with CSCR was similarly measured using a standard protocol. Subretinal fluid height was measured from the tip of the retinal pigment epithelium (RPE) to the outer border of the detached retina at the fovea.(155) All measurements were performed by a single experienced observer.

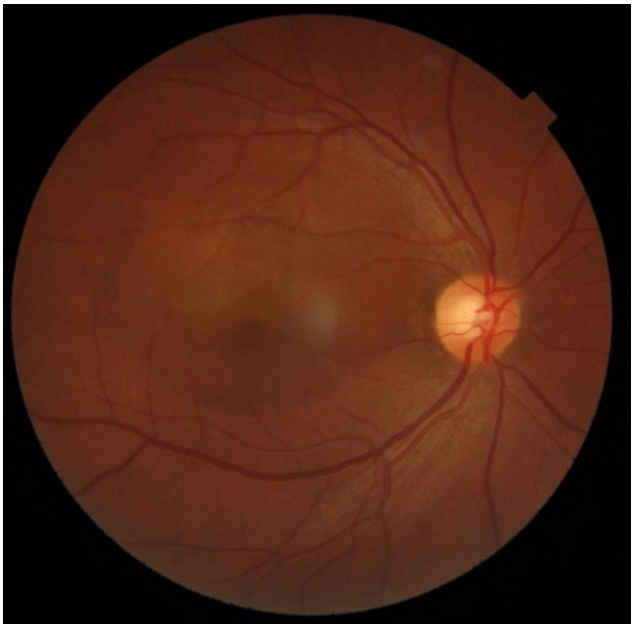


Figure 11: Colour fundus photograph of the CSCR eye of one of our patients

Figure 12: Swept Source OCT (DRI OCT TRITON Plus, TOPCON Inc, Tokyo, Japan) in our department

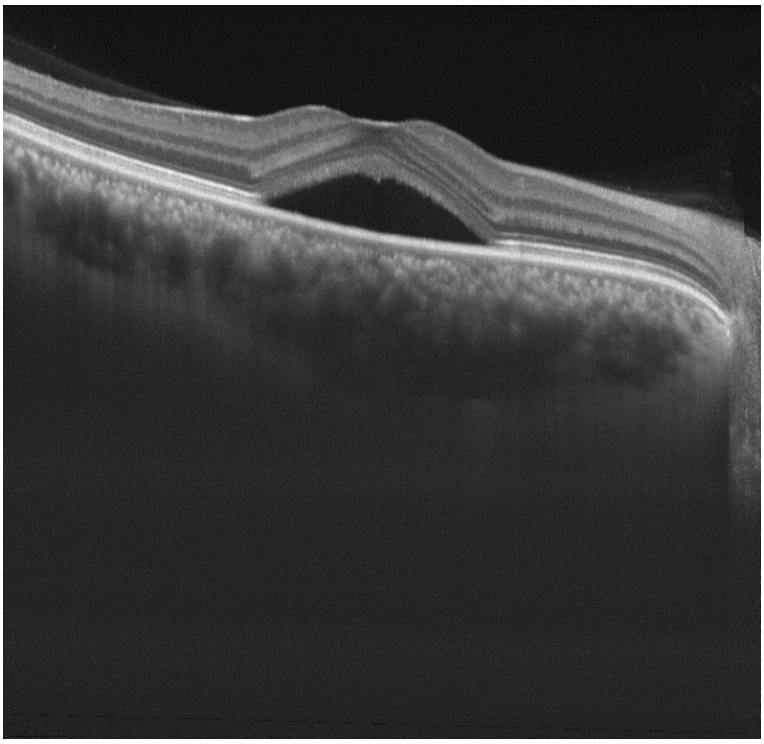


Figure 13: SS-OCT image of one of our patients showing CSCR and pachychoroid

Information regarding the clinical and sociodemographic profile of the participants, and about the potential risk factors for CSCR, was elicited using a Clinical Research Form. Psychological stress was assessed using the ten item version of Cohen Perceived Stress Scale (PSS-10).(Appendix 4) This is a widely used psychological instrument for measuring the perception of stress. The original English questionnaire was translated into Tamil and Hindi. Two versions of the translation in each language were obtained, which were then back translated into English. The English questionnaire, along with the

translations and back translations, were reviewed by five subject matter experts in each language (Tamil and Hindi), and the better of the two translations in each language was chosen. The Principal Investigator was trained to administer the questionnaire in a standard manner. It was piloted by the Principal Investigator in all three languages. The questionnaire was verbally administered to all the study participants by the Principal Investigator. Based on the score obtained after administering the questionnaire, patients were categorized into three as given below:

- 0 - 13: low stress
- 14 - 26: moderate stress
- 27 - 40: high stress

Data were collated and analyzed to compare the sub foveal choroidal thickness and stress scores of the two groups, and to study the correlation between sub foveal choroidal thickness and stress scores of the study subjects.

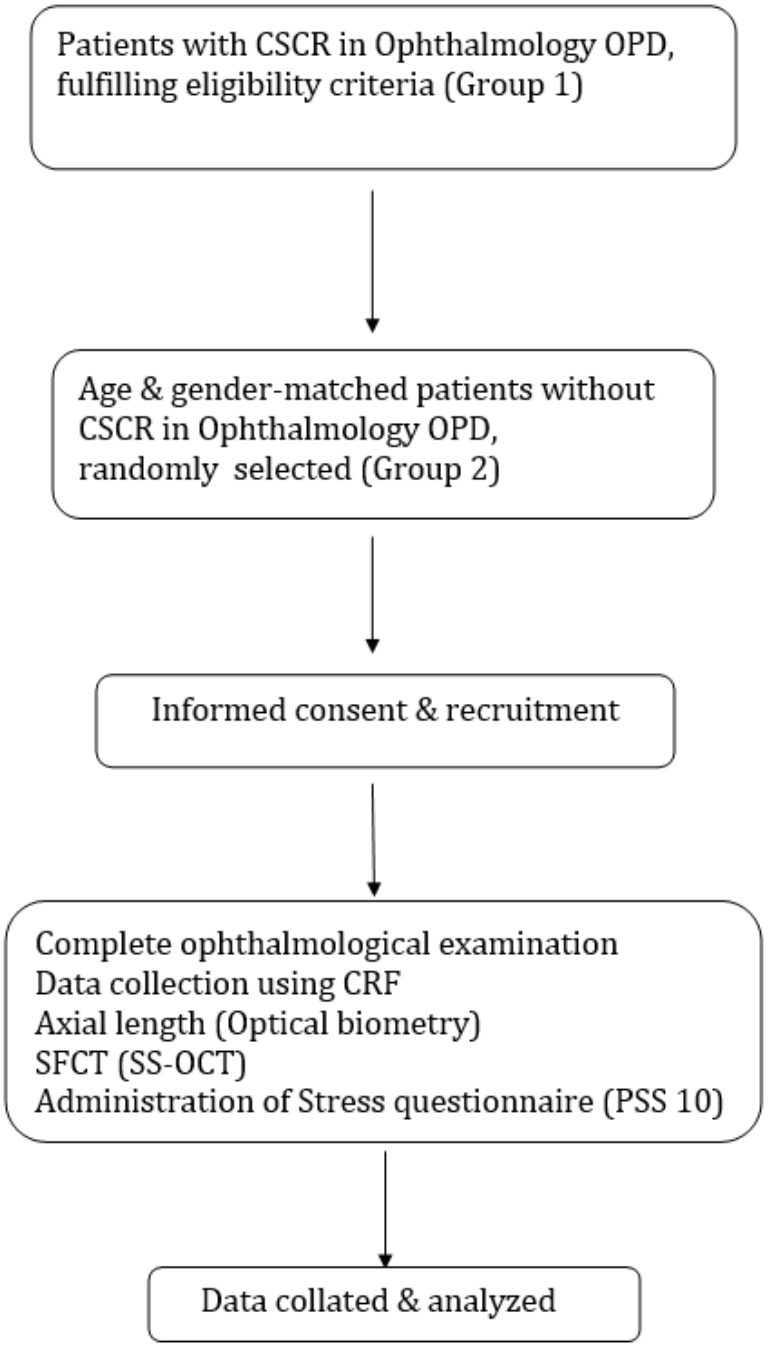


Figure 14: Diagrammatic algorithm of the study

Sample size calculation

Sample size based on primary objective [to compare the subfoveal choroidal thickness of the involved eye in patients with CSCR (Group 1) with that of the control eye in patients without CSCR (Group 2)]

Two Means - Hypothesis testing for two means	
Standard deviation in Group I subfoveal choroidal thickness - affected eye	109
Standard deviation in Group II subfoveal choroidal thickness - normal eye	71
Mean difference	166
Effect size	1.844444
Alpha error (%)	5
Power (1- beta) %	80
1 or 2 sided	2
Required sample size per group	5

With reference to the study by Maruko I et al.,(14) the mean subfoveal choroidal thickness of the affected eye was found to be 414±109 μm, and that of the age-matched, normal, control eyes was 248±71 μm. With a mean difference of 166 μm between the affected and the control eyes, with alpha error at 5% and power at 80% for a two-sided test, we had to study at least 5 patients with CSCR (Group 1) and 5 patients without CSCR (Group 2).

Formula

$$n = \frac{2{s_p}^2\left[Z_{1-\alpha/2} + Z_{1-\beta}\right]^2}{\mu_d^2}$$

$$s_p^2 = \frac{s_1^2 + s_2^2}{2}$$

Where,

s_1^2 : Standard deviation in the first group

s_2^2 : Standard deviation in the second group

μ_d^2 : Mean difference between the samples

α : Significance level

1- β : Power

Sample size calculation based on secondary objective (to study the correlation between the sub foveal choroidal thickness and stress scores of the study subjects)

Sample size calculation for the secondary objective was done using the correlation between sub foveal choroidal thickness and stress scores, assuming the correlation to be not less than 0.5, with the power at 80% and alpha error at 5% for a two sided test, we had to study at least 24 subjects in each group.

Regression methods - Correlation coefficient (testing for r=0)

Correlation coefficient	**0.6**	**0.5**	**0.7**
Power (1-beta) %	**80**	**80**	**80**
Alpha error %	**5**	**5**	**5**
1 or 2 sided	**2**	**2**	**2**
Required sample size	**14**	**24**	**8**

Formula

$$n = \frac{\left(Z_{1-\beta} + Z_{1-\frac{\alpha}{2}} \right)^2}{\left(\frac{r^2}{1 - r^2} \right)}$$

Where,

r : Correlation coefficient.

$Z_{1-\alpha/2}$: Desired confidence level

1-β : Power

Therefore, we studied 25 subjects in Group 1, and 50 subjects in Group 2 (1:2 ratio – for every patient with CSCR in Group 1, two age and gender-matched patients without CSCR in Group 2).

Data entry and analysis:

The data entry was done, using EpiData (Version 3.1). Statistical analysis was done using SPSS version 21.

Quantitative variables & Statistical methods:

Descriptive statistics were reported using Mean±SD for continuous variables. Categorical variables were reported using frequency and percentage. Continuous variables, which were normally distributed, were assessed using Independent samples t-test after checking for normality. Chi-square/ Fisher's exact test was used to compare categorical variables. The correlation between SFCT and stress scores of the study subjects was reported using Pearson's correlation coefficient.

Outcomes

Primary outcome:

Comparison of the subfoveal choroidal thickness of the involved eye in patients with Central serous chorioretinopathy - CSCR (Group 1), with that of the uninvolved fellow eye, and with that of age and gender-matched controls without CSCR (Group 2)

Secondary outcomes:

1. Comparison of the stress scores of patients with CSCR (Group 1) with that of the control group (Group 2)
2. Correlation between the subfoveal choroidal thickness and stress scores of the study subjects

Potential confounders/ suspected effect modifiers

Data regarding potential confounding factors/ suspected effect modifiers were obtained by history/ clinical examination/ laboratory investigations. The following were considered as potential confounders/ suspected effect modifiers: Age, gender, axial length, refractive error, hypertension, smoking, alcoholism, post-organ transplantation, pregnancy, endogenous hypercortisolism, Helicobacter pylori infection, obstructive sleep apnea, allergic airway disease, diabetes, collagen vascular disorders, cardiovascular disease, steroid intake, other medicines that have been implicated in the etiopathogenesis of CSCR (list appended – Appendix 6).

Group 1 and Group 2 were matched for age and gender.

Extremes of age, axial length and refractive error, pregnant women, patients on steroids, post-organ transplant patients, and patients with history or clinical features of endogenous hypercortisolism were excluded.

Data regarding all other potential confounders/ suspected effect modifiers were documented and analyzed.

Management of bias

The possibility of intra-observer bias at the time of measurement of sub foveal choroidal thickness (SFCT) using SS-OCT was minimized by taking a total of six readings (three readings each of the horizontal and vertical line scans) of each eye, and the mean of these six readings was taken as the final measurement of SFCT of each eye.

Diagnostic criteria/ definitions

Central serous chorioretinopathy (CSCR): CSCR is a chorioretinal disorder with systemic associations and multifactorial etiology, characterized by serous detachment of the neurosensory retina, which is usually located at the posterior pole.(1)

Anatomical definitions :

Macula

Macula was defined as the region within the major temporal blood vessels, having an approximate diameter of 5.5 mm.(90)

Peripapillary area

Peripapillary area was defined as the area within 1 disc diameter of the optic nerve, excluding the macula.(90)

Periphery

Periphery was defined as the area of the retina outside the macula and peripapillary region.(90)

Hypertension:

For this study, all subjects with history of hypertension, on medication, or with elevated blood pressures as defined below, were taken as hypertensive.

- Systolic blood pressure ≥ 140 mmHg or
- Diastolic blood pressure ≥ 90 mmHg

A minimum of two readings were taken at intervals of at least one minute, and the average of those readings was used to represent the patient's blood pressure. If there was more than 5 mmHg difference between the two readings, additional (one or two) readings were obtained, and the average of these multiple readings were taken.(156)

Smoking:

All participants were divided into the following four groups:

- Group 1 (Nil smoking) – participants who did not smoke at all
- Group 2 (Regular smoking) – participants who smoke more than once a week
- Group 3 (Occasional smoking) – participants who smoke less than once a week
- Group 4 (Quit smoking) – participants who stopped smoking at least six months earlier

Smoking was considered as positive in all those falling under Group 2.(157)

Alcoholism:

All participants were divided into the following four groups:

- Group 1 (Nil alcohol consumption) – participants who did not consume alcohol at all
- Group 2 (Regular alcohol consumption) – participants who consume alcohol more than once a week

- Group 3 (Occasional alcohol consumption) – participants who consume alcohol less than once a week

- Group 4 (Quit alcohol consumption) – participants who stopped alcohol consumption at least six months earlier

For the purpose of this study, alcoholism was considered as positive in all those falling under Group 2.

RESULTS

During the study period, from February 2018 to September 2019, 38 patients with Central serous chorioretinopathy were screened for recruitment into the study. Twenty five patients who fulfilled the eligibility criteria, were recruited into Group 1 of the study. Fifty randomly selected, age and gender-matched controls without CSCR comprised Group 2 of the study. Data obtained from 75 participants, including 25 cases and 50 controls, were analyzed, and the following results were obtained.(Figure 15)

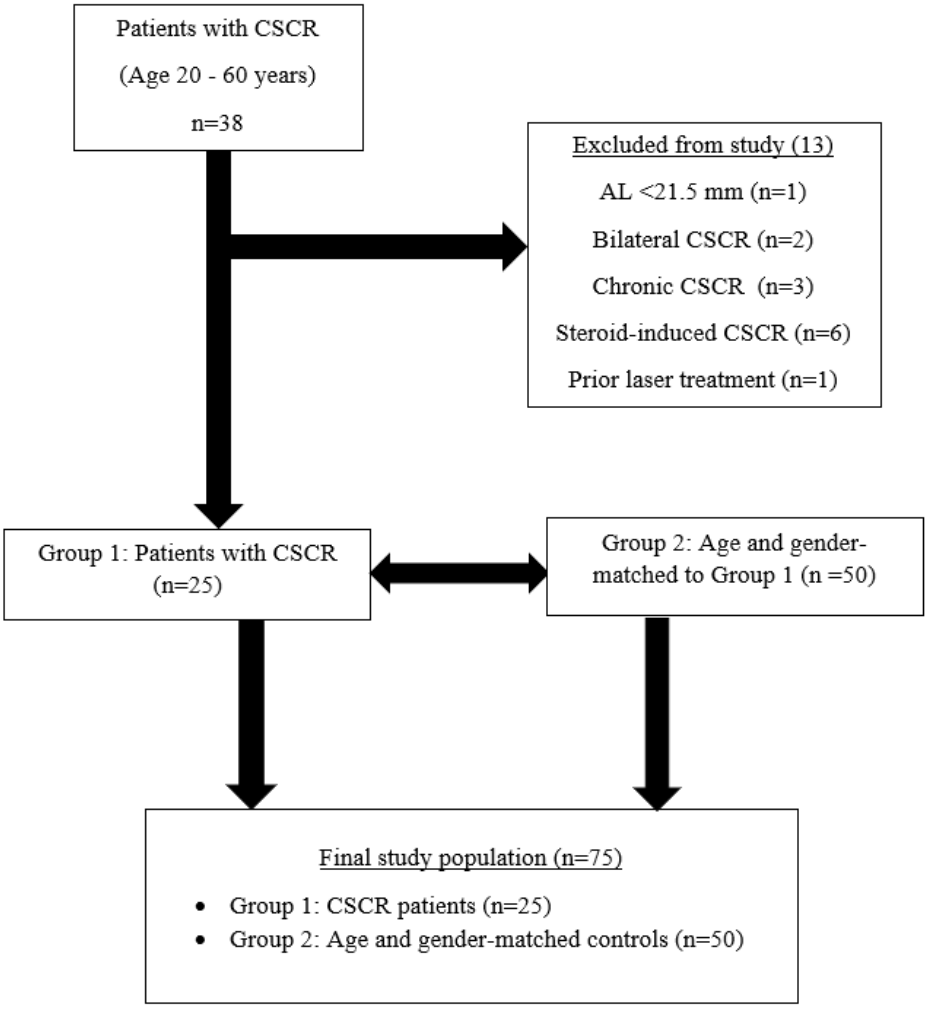


Figure 15: Flow chart of the study patient selection

Demographic characteristics

Age distribution

The age of patients in Group 1 (cases) ranged from 29 to 52 years. The age of controls (Group 2) was 2.5 years more or less than that of the cases. The mean (+/- SD) age in Group 1 and Group 2was38.80 +/- 5.89 years and 39.08 +/-5.79 years respectively (*P*=.85).

Table 1: Age distribution in the two groups

	N	**Mean**	**S.D**	**Min.**	**Max.**
Group 1	25	38.80	5.89	29	52
Group 2	50	39.08	5.79	29	53

(Age in years) *P*=.85

Gender distribution

Group 1 (cases) and Group 2 (controls) were gender-matched. Table 2 shows the gender distribution in the two groups.

Table 2: Gender distribution in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Male	21(84)	42(84)	63(84)
Female	4(16)	8(16)	12 (16)
Total	25	50	75

P=1.00

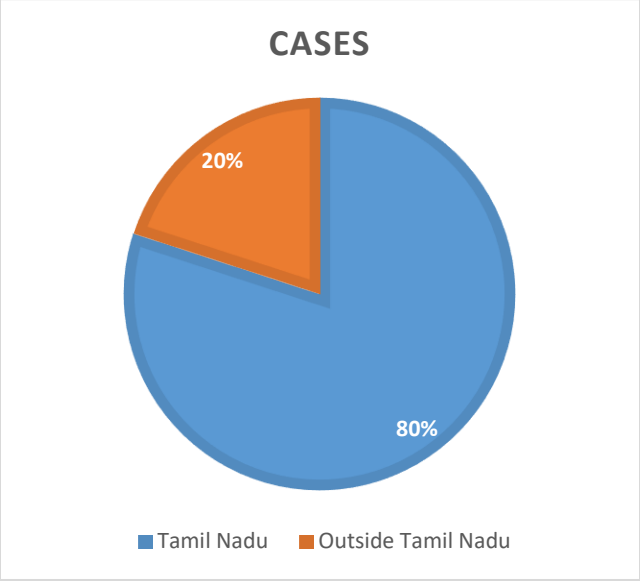
Place of residence

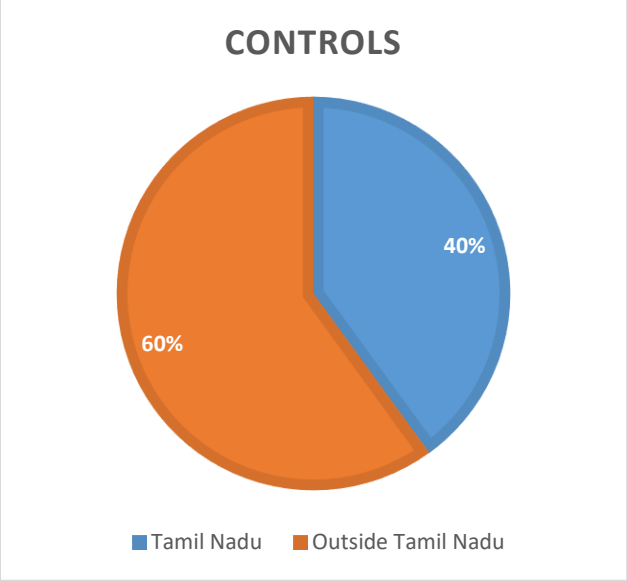
In Group 1, only five patients (20%) were from states outside Tamil Nadu, which included Bihar, Jharkhand, Karnataka, West Bengal, as well as from Bangladesh. In Group 2, out of the 50 controls, 30 (60%) were from states outside Tamil Nadu, like Andhra Pradesh, Bihar, Chhattisgarh, Jharkhand, Orissa, Tripura, West Bengal, as well as from Bangladesh.

Table 3: Place of residence

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Tamil Nadu	20(80)	20(40)	40(53.33)
Outside Tamil Nadu	5(20)	30(60)	35(46.66)
Total	25	50	75

P<.01





Educational status

Participants of the study were grouped into seven categories, based on their educational status, as per Modified Kuppuswamy's socio economic scale.(158) The difference in the educational status between Group 1 and Group 2 was not statistically significant (*P*=.22).

Table 4: Educational status of the two groups

	Group 1 n (%)	**Group 2 n (%)**
Profession/ honors	1(4)	0 (0)
Graduate/post graduate	8(32)	26(52)
Intermediate/post high school Diploma	4(16)	7(14)
High school certificate	4(16)	7(14)
Middle school certificate	5(20)	4(8)
Primary school certificate	1(4)	5(10)
Illiterate	2(8)	1(2)
Total	25	50

P=.22

Since CSCR has been proposed to be associated with higher educational status,(104) we further did a subgroup analysis, comparing the most educationally qualified categories (i.e., Profession/ honors and Graduate/ post graduate) in the two groups. In this study, we did not find a statistically significant difference between the two groups (*P*=.26).

Table 5: Subgroup analysis of educational qualification categories in the two groups

	Group 1 n (%)	**Group 2 n (%)**
Higher educational qualification	9(36)	26(52)
Lower educational qualification	16(64)	24(48)
Total	25	50

P=.26

Socio economic status

Participants of the study were grouped into five categories, based on Modified Kuppuswamy's socio economic scale.(158) The difference between Group 1 and Group 2 was not statistically significant (*P*=.29).

Table 6: Socio economic status of the two groups

	Group 1 n (%)	**Group 2 n (%)**
Upper	4(16)	6(12)
Upper middle	8(32)	27(54)
Lower Middle	8(32)	8(16)
Upper Lower	5(20)	8(16)
Lower	0(0)	1(2)
Total	25	50

P=.29

Since CSCR has been proposed to be associated with a higher socio-economic status,(104) we further did a subgroup analysis comparing the two upper categories (Upper and Upper middle class) between the two groups. In this study, we did not find a statistically significant difference between the two groups (*P*=.42).

Table 7: Subgroup analysis of socio-economic status in the two groups

	Group 1 n (%)	**Group 2 n (%)**
Higher socio economic Status	12(48)	33(66)
Lower socio economic Status	13(52)	17(34)
Total	25	50

P=. 42

Table 8 shows the baseline demographic profile of the two groups in the study.

Table 8: Demographic profile of the two groups

	Group 1 n (%) or Mean +/- SD	**Group 2 n (%) or Mean +/- SD**	**Total**	***P* value**
Age(years)	38.80 +/- 5.89	39.08 +/-5.79		*P*=.85
Male	21(84)	42(84)	63(84)	*P*=1.00
Female	4(16)	8(16)	12 (16)	
Tamil Nadu	20(80)	20(40)	40(53.33)	***P*<.01**
Outside Tamil Nadu	5(20)	30(60)	35(46.66)	
Higher educational status	9(36)	26(52)	35(46.66)	*P*=0.26
Lower educational Status	16(64)	24(48)	40(53.33)	
Higher socio-economic status	12(48)	33(66)	45(60)	*P*=0.42
Lower socio-economic status	13(52)	17(34)	30(40)	

Symptoms of CSCR patients

Among the patients with CSCR (Group 1), decrease in vision was the most common symptom, present in 19 patients (61%), followed by a positive central scotoma present in 11 patients (36%). In our study, only one patient (3%) experienced metamorphopsia. Some patients experienced more than one symptom.

Table 9: Symptoms of CSCR patients

	Number of patients n (%)
Decrease in vision	19 (61%)
Positive central scotoma	11 (36%)
Metamorphopsia	1 (3%)

Group 2 consisted of patients in Ophthalmology OPD, who were age and gender-matched to Group 1. It included patients who had come for a routine eye checkup, change of prescription of glasses, patients presenting for diabetic retinopathy screening, or minor ocular complaints. The following were the diagnoses in these patients: refractive error, presbyopia, allergic conjunctivitis, and no abnormality detected on ocular examination. Some patients had more than one diagnosis.

Table 10: Diagnosis in Group 2

	Number of patients
Within Normal Limits	13
Refractive Error	19
Presbyopia	19
Allergic conjunctivitis	1

Duration of symptoms

Duration of the symptoms of the patients in Group 1 ranged from a minimum of four days to a maximum of 110 days (median: 14 days).

Risk factors

Hypertension

In Group 1, three (12%) out of the 25 patients were hypertensive, and in Group 2, two (4%) out of the 50 patients were hypertensive. The difference between the two groups was not statistically significant (*P* =.33).

Table 11: Hypertension in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Hypertension	3 (12)	2(4)	5(6.66)
No hypertension	22(88)	48(96)	70(93.33)
Total	25	50	75

P=.33

Diabetes

In Group 1, two (8%) out of the 25 patients were diabetic, and in Group 2, seven (14%) out of the 50 patients were diabetic. The difference between the two groups was not statistically significant (*P*= .71).

Table 12: Diabetes in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Diabetes	2(8)	7(14)	9(12)
No Diabetes	23(92)	43(86)	66(88)
Total	25	50	75

P=.71

Smoking

There were no smokers in Group 1, whereas eight(16%) out of 50 controls in Group 2 smoked. However, the difference between the two groups was not statistically significant. (*P*= .09)

Table 13: Smoking in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Smoking	0(0)	8(16)	8(10.66)
No smoking	25(100)	42(84)	67(89.33)
Total	25	50	75

P =.09

Alcoholism

Alcoholism was noted in one (4%) out of the 25 cases in Group 1, and in two (4%) out of the 50 controls in Group 2. The difference between the two groups was not statistically significant (*P*=1.00).

Table 14: Alcoholism in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Alcoholism	1(4)	2(4)	3(4)
No alcoholism	24(96)	48(96)	72(96)
Total	25	50	75

P=1.00

Dyspepsia

None of the cases in Group 1 had dyspepsia, whereas in Group 2, two(4%) out of the 50 controls had dyspepsia. However, the difference between the two groups was not statistically significant (*P*=.55).

Table 15 : Dyspepsia in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Dyspepsia	0(0)	2(4)	2(2.66)
No dyspepsia	25(100)	48(96)	73(97.33)
Total	25	50	75

P=.55

Snoring

In Group 1, three(12%) out of the 25 cases snored, and in Group 2, two(4%) out of the 50 controls had snoring. The difference between the two groups was not statistically significant (*P*=.33).

Table 16 : Snoring in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Snoring	3(12)	2(4)	5(6.66)
No snoring	22(88)	48(96)	70(93.33)
Total	25	50	75

P=.33

Seasonal cough/ wheeze

Seasonal cough/ wheeze was present in two (8%) out of the 25 cases in Group 1, while one (2%) out of the 50 controls in Group 2 reported these symptoms. The difference between the groups was not statistically significant (*P*=.26).

Table 17: Seasonal cough/wheeze in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Seasonal cough/wheeze	2(8)	1(2)	3(4)
No seasonal cough/wheeze	23(92)	49(98)	72(96)
Total	25	50	75

P=.26

Cardio vascular disease

None of the cases in Group 1 had cardiovascular disease, while it was reported in one (2%) out of the 50 controls in Group 2.The difference between the groups was not statistically significant (*P*= 1.00).

Table 18: Cardiovascular disease in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
Cardio vascular disease	0(0)	1(2)	1(1.33)
No cardio vascular disease	25(100)	49(98)	74(98.66)
Total	25	50	75

P=1.00

Collagen vascular disorders

None of the patients in our study had collagen vascular disorders.

Medications

All medications taken by patients in both the groups were documented, and data pertaining to those medications that have been implicated in the etiopathogenesis of CSCRwere analyzed separately, to look for any statistically significant difference between the two groups. In our study, two(8%) patients in Group 1 were on such medications (one patient on psychopharmacological medications and one on antihistaminics), while none of the patients in Group 2 were on any medications that have been implicated in the etiopathogenesis of the disease. The difference between the two groups was not statistically significant.(*P*=.11)

Table 19: Table showing medications taken by patients in the two groups

	Group 1 n (%)	Group 2 n (%)
Antihistaminics	**1(4)**	**0(0)**
Psychopharmacological medications	**1(4)**	**0(0)**
Tegrital	0(0)	1(2)
OHA	2(8)	7(14)
Antihypertensives	2(8)	1(2)
Thyroxine	0(0)	2(4)
Flunarizine	0(0)	1(2)
No medications	19(76)	38(76)
Total	25	50

Table 20: CSCR relevant medications in the two groups

	Group 1 n (%)	**Group 2 n (%)**	**Total**
CSCR relevant medication	2(8)	0(0)	2(2.66)
No CSCR relevant medication	23(92)	50(100)	73(97.33)
Total	25	50	75

P=.11

Investigations and results

Refractive error

In Group 1 (cases), refractive error in the CSCR eyes ranged from -1.00 D Sphere to +2.00 D Sphere with a mean of +0.50 +/-0.67 D Sphere. In the fellow eyes,refractive error ranged from -1.75 D Sphere to +1.75 D Sphere with a mean of +0.39 +/-0.52D Sphere. The mean difference in refractive error between the two eyes was 0.39 +/- 0.45D Sphere.

In Group 2 (controls), refractive error in the right eyes ranged from -1.75 D Sphere to +2.00D Spherewith a mean of +0.33 +/-0.73D Sphere.Refractive error in the left eyes of controls ranged from -1.75 D Sphere to +2.00 D Sphere with a mean of +0.33 +/-0.75D Sphere. The mean difference in refractive error between the two eyes was 0.26 +/- 0.27D Sphere.

The right eye of the patients in Group 2 was taken as the ‘control eye’ for analysis of the comparison of the refractive error between the two groups.

There was no statistically significant difference in the refractive error, either between the CSCR eyes and the control eyes, or between the fellow eyes and the control eyes. The mean difference in refractive error between the two eyes of the patients in Group 1 and Group 2 was also comparable.(Table 21)

Table 21: Refractive error in the two groups

	Mean	**SD**	***P* value**
RE in CSCR eyes	+0.50	0.67	.33
RE in control eyes	+0.33	0.73	
RE in fellow eyes	+0.39	0.52	
RE in control eyes	+0.33	0.73	.72
RE difference b/w 2 eyes of patients (Group 1)	0.39	0.45	.12
RE difference b/w 2 eyes of patients (Group 2)	0.26	0.27	

RE: Refractive error was measured in Dioptre Sphere

Axial length

In Group 1 (cases), the axiallength in the CSCR eyes ranged from 21.6 mm to 24.0 mm, with a mean of 23.06 +/- 0.55 mm. In the fellow eyes, the axiallength ranged from 21.7 mm to 24.2 mm, with a mean of 23.13 +/- 0.58 mm. The mean difference in axial length between the two eyes was 0.14 +/- 0.11mm.

In Group 2 (controls),the axial length of the right eyes ranged from 22.0 mm to 24.3 mm, with a mean of 23.19 +/- 0.56 mm. In the left eyes, the axial length ranged from 21.9 mm to 24.3 mm,

with a mean of 23.20 +/- 0.59 mm. The mean difference in axial length between the two eyes was 0.09 +/- 0.08mm.

The right eye of the patients in Group 2 was taken as the 'control eye' for analysis of the comparison of the axial length between the two groups.

There was no statistically significant difference in axial length, either between the CSCR eyes and the control eyes, or between the fellow eyes and the control eyes. The mean difference in axial length between the two eyes of the patients in Group 1 and Group 2 was also comparable.(Table 22)

Table 22: Axial length in the two groups

		Minimum	**Maximum**	**Mean**	**SD**
Group 1	**CSCR eye**	21.6	24.0	23.06	0.55
	Fellow eye	21.7	24.2	23.13	0.58
Group 2	**Right eye**	22.0	24.3	23.19	0.56
	Left eye	21.9	24.3	23.20	0.59

Axial length was measured in millimetres(mm).

Table 23: Table comparing mean axial length in the two groups

	Mean	**SD**	***P* value**
AL in CSCR eyes	23.06	0.55	.36
AL in control eyes	23.19	0.56	
AL in fellow eyes	23.13	0.58	
AL in control eyes	23.19	0.56	.68
AL difference b/w 2 eyes of patients (Group 1)	0.14	0.11	.71
AL difference b/w 2 eyes of patients (Group 2)	0.09	0.08	

Axial length was measured in millimetres(mm).

Blood pressure

The mean(+/- SD) systolic blood pressure was 123.20 +/- 16.45 mm Hg in Group 1 patients with CSCR, and 106.40 +/- 11.25 mm Hg in Group 2 (controls). The difference between the twogroups was statistically significant **(*P*< .01)**.

The mean(+/- SD) diastolic blood pressure was 78.08 +/- 10.09 mm Hg in Group 1 patients with CSCR,and 70.80 +/- 8.47 mm Hg in Group 2 (controls). The difference between the twogroups was statistically significant **(*P*< .01)**.

Table 24: Blood pressure in the two groups

	Group 1(mean+/- SD)	**Group 2(mean+/- SD)**	***P* value**
Systolic BP	123.20 +/- 16.45	106.40 +/-11.25	**<.01**
Diastolic BP	78.08 +/- 10.09	70.80 +/-8.47	**<.01**

Blood pressure was measured in mm Hg.

Stress score

Stress scoring ranged from 0-40 as per Cohen's perceived stress scale (PSS-10). There was a significant difference in mean stress scores between Group 1 patients with CSCR and Group 2 patients without CSCR (***P*<.01**).

Table25: Stress scores in the two groups

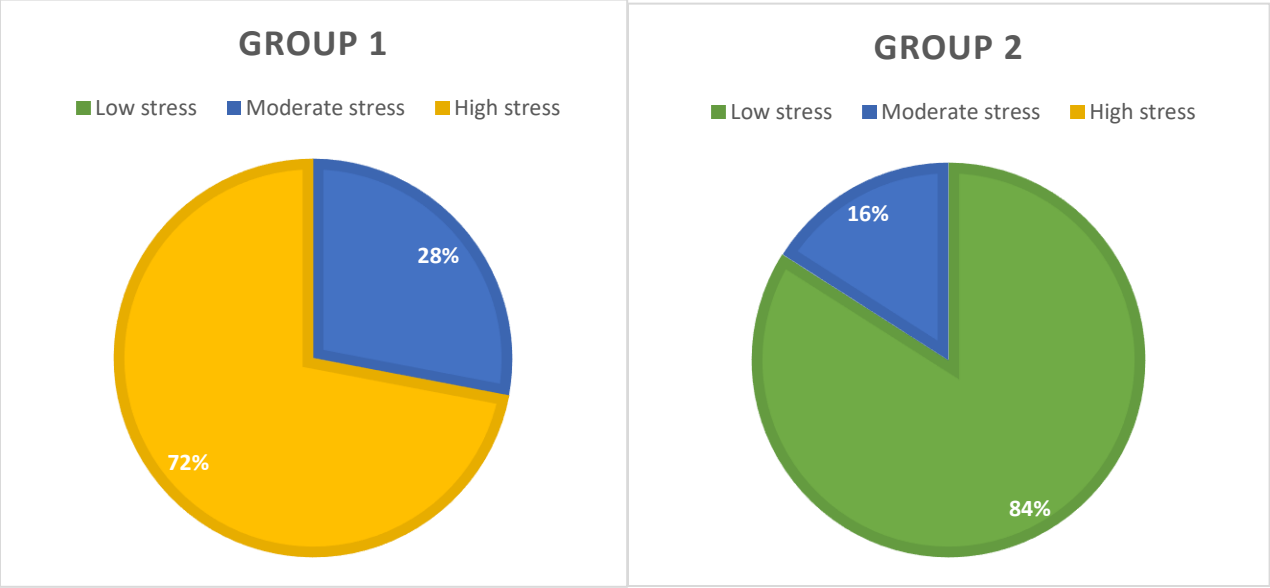
	n	**Minimum**	**Maximum**	**Mean**	**SD**	**P value**
Group 1	25	15	38	23.72	5.792	**<.01**
Group 2	50	6	20	11.12	3.173	

Based on the scores, patients were further classified into categories of Low, Moderate and High stress, as per PSS-10. Scores from 0 to 13 were categorized as 'low stress', 14 to 26 as'moderate stress', and 27 to 40 as'high stress'.There was a statistically significant difference between Group 1 and Group 2 with respect to stress categories (***P*< .01**).

Table 26: Stress categories in the two groups

	Group 1 n (%)	Group 2 n (%)
Low stress	0(0)	42(84)
Moderate stress	18(72)	8(16)
High stress	7(28)	0(0)
Total	25	50

***P*< .01**



Sub foveal choroidal thickness (SFCT)

The mean subfoveal choroidal thickness of CSCR eyes was greater than that of the control eyes (***P*<.01;** the right eye of controls in Group 2 was taken for analysis). We also found that the mean SFCT of the fellow eyes of CSCR patients was significantly higher than that of the control eyes

(***P*<.01**). However, there was no statistically significant difference in the mean SFCT of CSCR eyes and fellow eyes.(*P*=.24).

Table 27: Subfoveal choroidal thickness in the two groups

		Minimum	**Maximum**	**Mean**	**SD**
Group 1	**CSCR eyes**	249	546	421.00	78.34
	Fellow eyes	232	516	396.20	68.79
Group 2	**Right eyes**	204	394	314.24	52.48
	Left eyes	190	396	311.84	53.19

SFCT was measured in μm.

Table 28: Comparison of subfoveal choroidal thickness between the two groups

	Mean	**SD**	***P* value**
SFCT in CSCR eyes	421.00	78.34	**<.01**
SFCTin controleyes	314.24	52.48	
SFCT in fellow eyes	396.20	68.79	
SFCT in control eyes	314.24	52.48	**<.01**
SFCT in CSCR eyes	421.00	78.34	
SFCT in fellow eyes	396.20	68.79	.24

SFCT was measured in μm.

Serous Retinal Detachment (SRD)

Serous retinal detachment was measured at the fovea in all the CSCR eyes (Group 1). The height of the subretinal fluid ranged from 113 μm to 713 μm, with a mean of 310.08 +/-176.07 μm.

Table 29: Height of the subretinal fluid in CSCR eyes in Group 1

	N	Minimum	Maximum	Mean	SD
SRD	25	113	713	310.08	176.07

SRD was measured in μm.

Pigment Epithelial Detachment (PED)

Pigment epithelial detachment (PED) was noted on FFA and OCT images in Group 1, and on OCT images in Group 2 of the study.

Thirteen patients (52%) in the CSCR group had PED. Two out of these 13 patients had PED also in the fellow eye. In the control group, only one patient (2%) had PED.The difference between the two groups was statistically significant (***P*<.01**).

Table 30: Patients with PED in the two groups

	Group 1 n (%)	**Group 2 n (%)**
PED	13(52)	1(2)
No PED	12(48)	49(98)

***P*<.01**

Fundus Fluorescein Angiography (FFA) findings

Fundus Fluorescein Angiography (FFA) was done in 24 out of the 25 patients in Group 1, and the findings are described below.

Site of leak

Active leakage of dye was seen only in CSCR eyes. Out of the 24 patients who underwent FFA, 20 patients (83.33%) had a leak at the macula, two (8.33%) in the periphery, one (4.16%) in the peripapillary area, and no active leak was found in one patient (4.16%).

Table 31: Site of leak in FFA

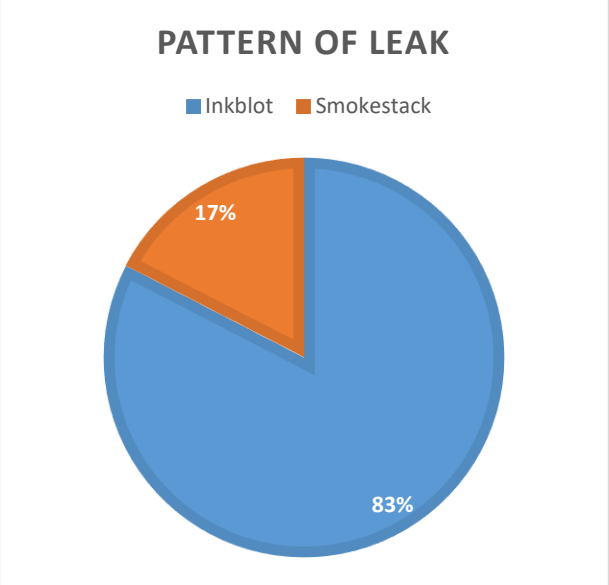
	Number of patients n (%)
Macula	20(83.33)
Periphery	2(8.33)
Peripapillary	1(4.16)
No active leak	1(4.16)
Total	24

Number of foci of leak

Out of the 24 patients who underwent FFA, 21 patients (87.5%) had a single focus of leak, two patients (8.33%) had two foci of leak, and as mentioned earlier, there was no active focus of leakage identified in one patient (4.16%). None of our study patients had more than two foci of leak, and none of the fellow eyes had foci of active leakage of dye.

Pattern of leak

Nineteen out of the 23 patients with active leakage (83%) had an inkblot pattern of leak, while four (17%) had a smokestack pattern of leakage of dye.



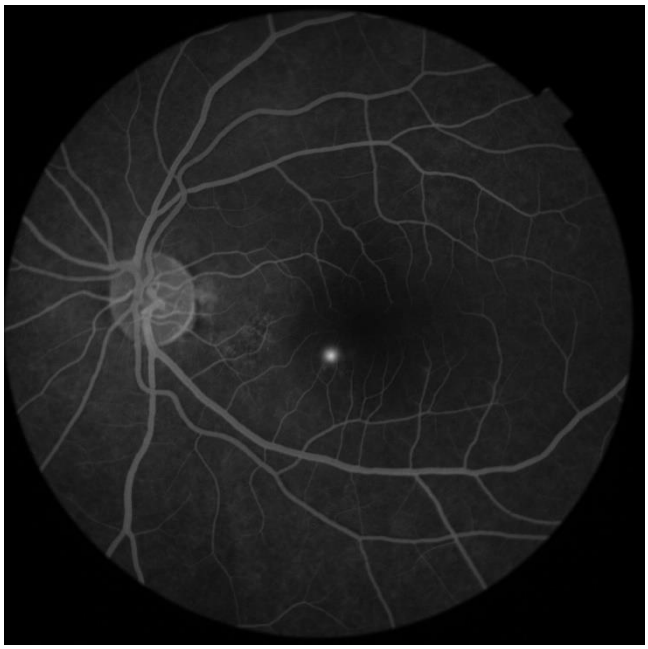


Figure 16: FFA image of one of our study patients showing inkblot pattern of leakage in the CSCR eye

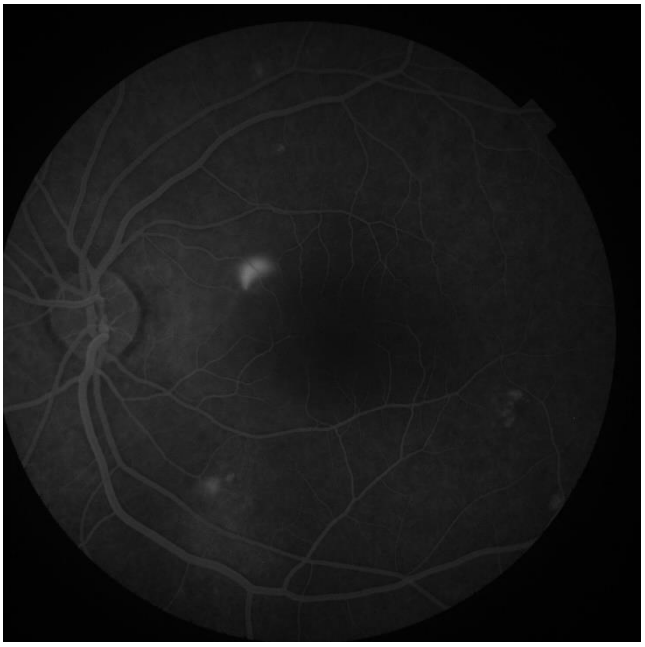


Figure 17: FFA image of one of our study patients showing smokestack pattern of leakage in the CSCR eye

Choroidal Neo Vascular Membrane (CNVM)

None of our study patients were noted to have a choroidal neovascular membrane.

Retinal pigment epithelial (RPE) atrophic changes

Window defects consistent with retinal pigment epithelial (RPE) atrophic changes were noted in the CSCR eye in 20 out of the 24 patients (83.33%) who underwent FFA. Macula was the most common site (18 patients), followed by the periphery (two patients). None of our study patients had RPE changes in the peripapillary area in the CSCR eye.

In the fellow eye, 15 patients (62.5%) had RPE atrophic changes. The changes were noted at the macula in 13 patients, in the peripapillary area in three patients, and in the periphery in two patients. Two out of the fifteen patients had RPE changes in more than one area.

There was no significant difference in the prevalence of RPE atrophic changes noted on FFA, between the CSCR eye and the fellow eye ($P = .22$).(Table 32)

Table 32: RPE changes in the CSCR eyes and fellow eyes

	CSCR eyes n (%)	**Fellow eyes n (%)**	**Total**
RPE changes	20(83.33)	15(62.5)	35 (72.92)
No RPE changes	4(16.66)	9(37.5)	13 (27.08)
Total	24	24	48

$P = .22$

Correlation between subfoveal choroidal thickness (SFCT) and stress scores

There was a strong positive correlation between the subfoveal choroidal thickness (SFCT) and the stress scores of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.85, ***P* <. 01**), although no significant correlation was found in the individual groups (r = -0.33, *P*= .11 in Group 1 and r = -0.19, *P* = .19 in Group 2).

Correlation between subfoveal choroidal thickness (SFCT) and blood pressure

There was a strong positive correlation between the subfoveal choroidal thickness (SFCT) and both the systolic (SBP) and diastolic blood pressure (DBP) of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.92, ***P* < .01** for SBP, r =0.901, ***P* < .01** for DBP), although no significant correlation was found in the individual groups (r = -0.12, *P* = .56 for SBP in Group 1 and r = -0.11, *P* = .47 for SBP in Group 2, r = -0.26, *P* = .2 for DBP in Group 1 and r= -0.11, *P* = .44 in Group 2).

Correlation between blood pressure and stress scores

There was a strong positive correlation between the stress scores and both the systolic (SBP) and diastolic blood pressure (DBP) of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r = 0.88, ***P* < .01** for SBP and r = 0.88, ***P* < .01** for DBP), although no significant correlation was found in the individual groups (r = -0.19, *P*= .37 for SBP in Group 1 and r = 0.02, *P* = .92 for SBP in Group 2 , r = -0.007, *P* = .97 for DBP in Group 1 and r = 0.05, *P* = .71 for DBP in Group 2).

DISCUSSION

Central serous chorioretinopathy (CSCR) is a disease with a multifactorial etiology. Numerous studies around the world have looked at various aspects of the disease. Most of our present day knowledge regarding the disease has evolved after the advent of advanced choroidal and retinal imaging technologies like Swept source and Enhanced depth imaging OCT, fundus fluorescein angiography and indocyanine green angiography. The aim of our study was to evaluate the role of choroidal thickness and psychological stress in patients with Central serous chorioretinopathy (CSCR). We studied 25 patients with CSCR (Group 1) and 50 age and gender-matched controls (Group 2).

Demographic profile

The baseline demographic profile of the two groups was comparable. The two groups were age and gender-matched. CSCR is classically described as a disease of the young to middle-aged, with a male preponderance. A testosterone-mediated pathway with direct influence of androgens has been postulated in the pathogenesis of CSCR.(97,99) Various studies have confirmed the male preponderance of the disease, and reported a mean age of incidence around 35 to 40 years.(40–42) We also found a male preponderance (88%) in our study. The mean age of onset of CSCR in our study was 38.80 +/- 5.89 years.

As our hospital is a tertiary care center, catering to patients from all over India, as well as from neighboring countries of the Indian subcontinent, the patients in both groups of our study came from all over India, as well as from Bangladesh. However, 80% of the

patients in Group 1 were from Tamil Nadu, while in Group 2, only 40% were from Tamil Nadu. The difference between the two groups was found to be statistically significant (***P*<.01**). This was probably because the patients with acute CSCR (less than four months) in Group 1, would have come to our hospital from nearby areas, primarily for their specific CSCR-related ocular complaints, while the majority of the patients in Group 2 (age and gender-matched controls) were those who had come for a routine eye examination, and did not have any major ocular morbidities. Patients with ocular diseases such as glaucoma, uveitis, diabetic retinopathy or significant cataract, who came from outside Tamil Nadu, seeking tertiary care ophthalmic services, would have been excluded from the study, as these diseases were part of the exclusion criteria of the study.

In our study, we compared the educational and socio-economic status between Group 1 and Group 2, and we found that there was no statistically significant difference between the two groups (*P*=.22 and *P* =.29 respectively).Very few studies have looked at the association of educational or socio economic status with CSCR. A study by Chatziralli et al. found higher educational status and income to be associated with CSCR.(113) In this context, we further did a sub group analysis comparing the higher educational and socio economic status categories in the two groups; however, we could not find a statistically significant difference (*P*=.2 and *P* =.42 respectively).

Potential confounders/ suspected effect modifiers/ risk factors

The following were considered as potential confounders/ suspected effect modifiers in our study: age, gender, axial length, refractive error, hypertension, smoking, alcoholism, post-organ transplantation, pregnancy, endogenous hypercortisolism, Helicobacter pylori

infection, obstructive sleep apnea, allergic airway disease, diabetes, collagen vascular disorders, cardiovascular disease, steroid intake and other medicines that have been implicated in the etiopathogenesis of CSCR.(Appendix 6)

As mentioned earlier, Group 1 and Group 2 were matched for age and gender. Extremes of age, axial length and refractive error, pregnant women, patients on steroids, post-organ transplant patients, and patients with history or clinical features of endogenous hypercortisolism were excluded. Data regarding all other potential confounders/suspected effect modifiers/ risk factors were meticulously documented and analyzed. We did not find a statistically significant difference between the two groups with respect to any of the factors given below.

Hypertension: Several investigators have studied the role of hypertension in the etiopathogenesis of CSCR.(101,102,104,118) Untreated hypertension results in alteration in choroidal circulation, and contributes to CSCR by causing arteriosclerotic changes in choroidal vessels, leading to their constriction. Venkatesh et al. found that the mean systolic and diastolic blood pressure of CSCR patients were more than that of the control group (*P*=.007).(159) There was no statistically significant difference in the number of hypertensive patients between the two groups in our study (*P*=.33). However, we found a statistically significant difference between the two groups in both the mean systolic blood pressure (123.20 +/- 16.45mm Hg in Group 1 versus 106.40 +/-11.21mm Hg in Group 2; ***P*<.01**), and the mean diastolic blood pressure (78.08 +/- 10.09 mm Hg in Group 1 versus 70.80 +/-8.47 mm Hg in Group 2, ***P*<.01**).

Diabetes mellitus: The role of diabetes mellitus in CSCR has also been studied. Diabetes is proposed to be associated with a thinner choroid.(72,73) Similar to its effect on other blood

vessels in the human body, diabetes causes microvascular changes within the choroidal vasculature, thus compromising the blood supply to the choroid. However, its role in CSCR has been debatable, and various studies have reported conflicting results. Chatziralli et al. found no association of diabetes with CSCR,(104) whereas Haimvoci et al. found an association of diabetes mellitus with CSCR (P<.0001) after multivariate analysis.(102) In our study, we could not find a statistically significant difference between the two groups with respect to diabetes (P= .71).

Smoking and alcohol have been postulated as risk factors for CSCR. Substance abuse is known to be a behavioral adaptation to psychological stress.(101) Additionally, both alcohol and nicotine hamper the nitric oxide-mediated vasodilation of the choroidal vessels, in turn, resulting in their constriction.(77,106) Some investigators have found smoking(102,104) and alcohol(102) to be risk factors for CSCR. However, in our study, we could not find a statistically significant difference between the two groups with respect to smoking and alcohol.(P = .09 and P= 1.0 respectively).

Helicobacter pylori infection: Many studies have evaluated the association of Acid peptic disease with CSCR. Acid peptic disease and Helicobacter pylori infection of the gastro intestinal tract have been described as risk factors for CSCR in various studies.(102,104) The mechanism is postulated to be a molecular mimicry between the bacterial cell wall antigen and the homologous proteins on the endothelium of the choroidal vessels.(112,113) In our study, we assessed the symptom of dyspepsia as a surrogate marker for Acid peptic disease and H. pylori infection, and we found no statistically significant difference between the two groups (P=0.55). However, most studies that have evaluated this association have included chronic cases of

CSCR, whereas our study population was comprised of CSCR patients within four months of onset of the symptoms of the disease.

Obstructive sleep apnea (OSA) has been proposed as a risk factor for CSCR, although the exact pathogenetic mechanism has not been fully understood. Increased sympathetic activity has been shown to occur in OSA, which in turn, increases the cortisol levels, predisposing to the development of CSCR.(115) Studies by Kloos et al. and Chatziralli et al. have found an association between OSA and CSCR.(104,115) However, the study by Brodie et al. failed to show such an association (P=1.00).(116) In our study, we took the symptom of snoring as a surrogate marker for OSA, and we did not find a statistically significant difference between the two groups (P=.33).

Allergic airway disease: The association of CSCR with asthma has been proposed to be related to the chronic use of steroids in these patients.(117) Studies on this subject have produced conflicting results. Tittle et al. found no association between asthma and CSCR in their study.(118) However, Haimovici et al. found an association in their study, after stepwise logistic regression.(102) In our study, we used the symptom of wheeze/ seasonal cough as a surrogate marker for allergic airway disease. We did not find a statistically significant difference between the two groups (P=.26). It is possible that some patients with asthma were excluded from the study, as use of steroid medications was part of the exclusion criteria for participation in our study.

Cardiovascular disease: The mechanism of association of cardiovascular disease with CSCR is not fully understood, but has been attributed to the imbalance between coagulation and coagulysis.(119,120) In our study, we did not find a statistically significant difference between

the two groups with respect to cardiovascular disease (*P*=1.00). Our results are consistent with the results of the study by Chatziralli et al., in which the authors did not find an association between coronary artery disease and CSCR on multivariate analysis.(104)

Collagen vascular diseases: Some studies have documented an association of CSCR with auto immune diseases like collagen vascular diseases through a steroid-mediated mechanism.(102,104) We did not have any patients with collagen vascular diseases either in Group 1 or Group 2 of our study.

Medications: Various medications like psychopharmacological medications, anti-histaminics, antacids, anti-reflux medications, phosphodiesterase-5 inhibitors and sympathomimetics have been implicated in the etiopathogenesis of CSCR. Psycho pharmacological medications are commonly used in cases of psychological stress, which in itself, is a risk factor for CSCR. Anti-histaminics are used for the treatment of allergic airway disease, and antacids/ anti-reflux medications are used in the management of acid peptic disease, which are again risk factors for CSCR. Phosphodiesterase-5 inhibitors like Sildenafil are used in the treatment of erectile dysfunction, and they cause an engorgement of choroidal vessels.(127) Tittl et al. found an association of psychopharmacological medications with CSCR.(118) Haimovici et al. found no association of antihistaminic medications with CSCR.(102) In our study, two (8%) out of the 25 patients in Group 1 were on CSCR-relevant medications, and none of the patients from Group 2 were on any such medications. There was no statistically significant difference between the two groups (*P*= .11).

Refractive error: Subfoveal choroidal thickness (SFCT) is influenced by ocular parameters like refractive error and axial length. Myopia has been found to be associated with a thinner

choroid.(52,65) The Beijing Eye Study demonstrated a mean decrease in SFCT of 15 μm for every 1 Dioptre of myopia.(65) Another study by Ikuno et al. found 9.3 μm of thinning in SFCT for every dioptre of myopia.(52) In the study by Arora et al. on 84 CSCR eyes, 69 fellow eyes and 112 normal control eyes, the mean refractive error in CSCR eyes was +0.49 ± 0.70 D sphere, fellow eyes was +0.45 ± 0.73 D sphere, and normal eyes was +0.40 ± 0.73 D sphere.(13) This study had excluded patients with more than +/- 2 Dioptres of refractive error. Other studies had included subjects with refractive error up to -6 Dioptres, and therefore, obtained a higher mean myopic refractive error.(8,87)

In our study, we excluded patients with refractive error more than 2 Dioptres of myopia or hypermetropia in either eye, or a difference of more than 1dioptre between the two eyes, in order to minimize refractive error-induced variability in choroidal thickness. In Group 1 (cases), refractive error in the CSCR eyes ranged from -1.00 D Sphere to +2.00 D Sphere with a mean of +0.50 +/-0.67 D Sphere. In the fellow eyes, refractive error ranged from -1.75 D Sphere to +1.75 D Sphere with a mean of +0.39 +/-0.52D Sphere. The mean difference in refractive error between the two eyes was 0.39 +/- 0.45D Sphere.

In Group 2 (controls), refractive error in the right eyes ranged from -1.75 D Sphere to +2.00D Sphere, with a mean of +0.33 +/-0.73D Sphere. Refractive error in the left eyes of controls ranged from -1.75 D Sphere to +2.00 D Sphere with a mean of +0.33 +/-0.75D Sphere. The mean difference in refractive error between the two eyes was 0.26 +/- 0.27D Sphere.

The right eye of the patients in Group 2 was taken as the ‘control eye’ for analysis of the comparison of the refractive error between the two groups.

There was no statistically significant difference in the refractive error, either between the CSCR eyes and the control eyes (*P*=.33), or between the fellow eyes and the control eyes (*P*=.72). The mean difference in refractive error between the two eyes of the patients in Group 1 and Group 2 was also comparable (*P*=.12).

Axial length: Increase in axial length causes decrease in the choroidal thickness.(65,66) In the study by Li et al., every 1 mm increase in axial length decreased the SFCT by 58.2μm.(66) According to the Beijing Eye Study, SFCT decreased by 32 μm for every 1 mm increase in axial length.(65) In our study, we only included patients with axial length between 21.5 mm and 24.5 mm in either eye, and less than 0.5 mm difference in axial length between the two eyes, in order to minimize axial length-induced variation in choroidal thickness. The mean axial length was 23.06 +/- 0.55 mm in the CSCR eyes, 23.13 +/- 0.58 mm in the fellow eyes, and 23.19 +/ 0.56 mm in the control eyes. Our results were comparable to the study by Arora et al., who reported the mean axial length of CSCR eyes, fellow eyes and normal control eyes as 23.77 ± 0.45 mm, 23.80 ± 0.45 mm, and 23.70 ± 0.48 mm, respectively.(13) In our study, there was no statistically significant difference in axial length, either between the CSCR eyes and the control eyes (*P*=.36), or between the fellow eyes and the control eyes (*P*=.68). The mean difference in axial length between the two eyes was 0.14 +/- 0.11 mm in Group 1, and that in Group 2 was 0.09 +/- 0.08 mm and the two groups were similar (*P*=0.71).

Imaging characteristics of CSCR

Various studies have looked at the angiographic characteristics of acute CSCR. The most common site of leakage on FFA is the macula.(45,89) Inkblot pattern of leakage is more than the smokestack pattern.(89) Unifocal leakage is more frequent than multiple foci of leakage.(89) In our study also, macula was the most common site of leakage of the dye (83.33%). 87.5% of the patients had a single focus of leak. 83% of the patients had an inkblot pattern of leakage. 83.33% of the patients had RPE changes in the CSCR eye and 62.5% had RPE changes also in the fellow eye. There was no statistically significant difference between the CSCR eyes and the fellow eyes with respect to RPE changes (P= .22). The presence of RPE changes in the fellow eyes of patients with unilateral CSCR reiterates the concept that the pathophysiology of CSCR involves both eyes.

Subfoveal choroidal thickness (SFCT)

After the advent of advanced OCT technology which enabled imaging of the choroid, numerous studies have been carried out around the world to study the choroidal thickness in CSCR eyes. CSCR has been described as a disease belonging to the pachychoroid disease spectrum. Various studies have shown an increase in choroidal thickness in eyes with CSCR.(8,10,13,52,87,88) Furthermore, it has been found that SFCT in the fellow eyes was also thicker as compared to the control eyes.(13,87) Arora et al., in their study, reported the mean SFCT of CSCR eyes, fellow eyes and normal eyes to be 429 ± 74.18 μm, 360 ± 57.99 μm and 301.80 ± 46.59 μm respectively.(13)

In our study, the mean SFCT of the CSCR eyes, fellow eyes and the normal control eyes was 421 +/- 78.34 μm, 396.24 +/-52.48 μm and 314.24 +/-52.48 μm respectively. The mean SFCT of the CSCR eyes was significantly greater than that of the control eyes **(*P*<.01**). The mean SFCT of the fellow eyes was also significantly higher than that of the control eyes **(*P*<.01).** However, there was no statistically significant difference in the mean SFCT between the CSCR eyes and the fellow eyes (*P* = .24), again reiterating the concept of bilaterality of the pathophysiology of CSCR.

Many studies have found a statistically significant difference in the mean SFCT between the CSCR eyes and the fellow eyes.(10,13,14) Some of these studies had included patients with both acute and chronic CSCR. Maruko et al., in their study, demonstrated choroidal vascular hyperpermeability on ICG angiography in 23 (59.0%) fellow eyes of the 39 patients with acute CSCR, and twenty (74.1%) fellow eyes of the 27 patients with chronic CSCR. The fellow eyes with choroidal vascular hyperpermeability on ICGA showed a thicker mean SFCT as compared to the fellow eyes without choroidal vascular hyperpermeability (P < .001).(14) In our study, we only included patients with acute CSCR (within four months of onset of CSCR-related symptoms), and we did not do ICG angiography.

In our study, 83.33% of the patients had RPE changes in the CSCR eye and 62.5% had RPE changes also in the fellow eye, and there was no statistically significant difference between the CSCR eyes and the fellow eyes with respect to RPE changes (*P*= .22). The presence of comparable RPE changes and increased choroidal thickness in the fellow eyes of patients with unilateral CSCR reiterates the concept that the underlying pathophysiological changes leading to CSCR involve both the eyes of the patient. However, one eye tends to manifest the disease at a

particular point in time. The fellow eye may have been involved in the past, or may manifest the disease in the future, if the underlying etiopathological factors are not appropriately addressed.

Stress and CSCR

The association of CSCR with psychological stress and Type A personality has been extensively studied. Stress and Type A personality are associated with endogenous hypercortisolism. Stress activates the hypothalamic-pituitary-adrenal axis, causing increased secretion of cortisol.(24,128)

Various studies, using standard stress assessment tools, have found the stress scores to be significantly elevated in CSCR patients as compared to the normal population.(21,25,28,130,131) Economic crisis in Greece had led to a lot of new and recurrent cases of CSCR.(28) High stress job profiles were found to be prone to develop CSCR.(132) The occurrence of a disturbing psychological event prior to the onset of disease has also been observed,(26) along with inadequate coping mechanisms to the various psychosomatic factors in patients with CSCR.(129)

In our study, we used the Cohen Perceived Stress Scale (PSS-10) to assess the stress scores, and found significantly higher stress scores among the patients in the CSCR group (Group 1). The mean stress score was 23.72 +/- 5.792 in Group 1 and 11.12 +/- 3.173 in Group 2 (***P*<.01**). Based on the stress scores, the subjects were further classified into three categories (low , moderate and high stress), and we found a statistically significant difference between the two groups (**P < .01).** The results of our study were consistent with all the previous studies on this subject, thus reiterating the role of psychological stress in the etiopathogenesis of CSCR.

Correlation between stress and subfoveal choroidal thickness

One of our objectives was to study the correlation between stress and choroidal thickness. To the best of our knowledge, there have been no studies so far, which have looked at such a correlation. In our study, we found a strong positive correlation between the subfoveal choroidal thickness (SFCT) and the stress scores of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.85, ***P*<. 01**).

We also found a strong positive correlation between the sub foveal choroidal thickness (SFCT) and both the systolic (SBP) and diastolic blood pressure (DBP) of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.92, ***P* < .01** for SBP, r =0.901, ***P*< .01** for DBP).

Moreover, there was a strong positive correlation between the stress scores and both the systolic (SBP) and diastolic blood pressure (DBP) of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.88, ***P* < .01** for SBP and r =0.88, ***P*< .01** for DBP).

Undoubtedly, psychological stress continues to be a major risk factor for CSCR. Stress is also known to predispose to hypertension, but the exact mechanism is unclear. It has been proposed to be through the constant activation of the sympathetic system by the stress hormones.(160) Studies have also shown that young patients undergoing stress are more likely to develop essential hypertension as they approach midlife.(161) Various investigators have found that hypertension may also be an independent risk factor for CSCR.(102,159) Therefore, stress and hypertension may be highly inter-dependent factors that play a major role in the etiopathogenesis of the pachychoroid-related changes leading to CSCR.

Various modalities of management of CSCR have been tried with variable results. Concerns about chances of recurrence and adverse effects of treatment continue. The fact remains that unless the risk factors predisposing to the disease are appropriately addressed, the management may be inadequate, and the disease may recur and even become chronic, with subsequent risk of permanent visual impairment.

In the current scenario, systemic morbidities like cardiovascular disease and cerebrovascular accidents are on the rise, and rising levels of psychological stress have been implicated as one of the major risk factors. Unemployment, financial burden, family disputes, long working hours, quest for excellence, lack of a social support system and the changing sociocultural scenario are some of the causes for increase in psychological stress levels. Hence, stress management is the need of the hour.

Therapeutic strategies should target measures to relieve stress and equip the affected individuals to effectively manage stress. There is a lacuna in literature regarding effective stress management measures in patients with CSCR. Yoga, meditation, prayer, lifestyle modification, development of a new hobby, walking or other forms of physical exercise or sports and psychological counselling are various methods that could be suggested. Involvement of the services of a psychiatrist or psychologist in the management of patients with CSCR would be of the utmost importance. Adequate long term follow up and continued provision of holistic care are also important in the management of these patients.

CONCLUSIONS

- The mean subfoveal choroidal thickness of the CSCR eyes, fellow eyes and control eyes was 421 +/- 78.34 μm, 396.24 +/-52.48 μm and 314.24 +/-52.48 μm respectively.
- The mean SFCT of the CSCR eyes was significantly greater than that of the control eyes **(*P*<.01**).
- The mean SFCT of the fellow eyes was also significantly higher than that of the control eyes **(*P*<.01).**
- There was no statistically significant difference in the mean SFCT between the CSCR eyes and the fellow eyes (*P* = .24). 83.33% of the patients had RPE changes in the CSCR eye and 62.5% had RPE changes also in the fellow eye, and there was no statistically significant difference between the CSCR eyes and the fellow eyes with respect to RPE changes (*P*= .22). The presence of comparable RPE changes and increased choroidal thickness in the fellow eyes of patients with unilateral CSCR reiterates the concept that the underlying pathophysiological changes leading to CSCR involve both the eyes of the patient.
- The mean stress score of patients with CSCR (Group 1) was higher than that of age and gender-matched controls (Group 2), with a statistically significant difference between the two groups (23.72 +/- 5.79 versus 11.12 +/- 3.17, ***P* < .01**). Based on the stress scores, the patients were further classified into three categories

(low , moderate and high stress), and we found a statistically significant difference between the two groups also with respect to stress categories (**P < .01).**

- We found a statistically significant difference between the two groups in both the mean systolic blood pressure (123.20 +/- 16.45mm Hg in Group 1 versus 106.40 +/-11.21mm Hg in Group 2; ***P*<.01**), and the mean diastolic blood pressure (78.08 +/- 10.09 mm Hg in Group 1 versus 70.80 +/-8.47 mm Hg in Group 2, ***P*<.01**). However, there was no statistically significant difference in the number of hypertensive patients between the two groups in our study (*P*=.33).
- We found a strong positive correlation between the subfoveal choroidal thickness (SFCT) and the stress scores of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.85, ***P*<. 01**).
- There was a strong positive correlation between the subfoveal choroidal thickness (SFCT) and both the systolic (SBP) and diastolic blood pressure (DBP) of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.92, ***P*<.01**for SBP, r =0.901, ***P*< .01** for DBP).
- There was a strong positive correlation between the stress scores and both the systolic (SBP) and diastolic blood pressure (DBP) of the study population (n= 75 patients, including Group 1 and 2), using Pearson's correlation coefficient (r= 0.88, ***P*<.01**for SBP and r =0.88, ***P*< .01** for DBP).

Our study has reiterated the identity of CSCR as part of the pachychoroid disease spectrum. CSCR is a bilateral disease, related to a thick choroid with altered histopathological characteristics, closely associated with autonomic dysregulation of the choroidal vasculature.

Our observation that the fellow eyes of patients with unilateral CSCR have comparable RPE changes and increased choroidal thickness, reiterates the concept that the underlying pathophysiological changes leading to CSCR involve both the eyes of the patient. One eye may manifest the disease at a particular point in time. The fellow eye may have been involved in the past, or may manifest the disease in the future, if the underlying etiopathological factors are not appropriately addressed.

CSCR is a disease with multifactorial etiopathogenesis. Stress and hypertension may be highly inter-dependent factors that play a major role in the etiopathogenesis of the pachychoroid-related changes leading to CSCR. Our study has shown a strong positive correlation of stress and blood pressure with choroidal thickness. Although generally self-limiting, CSCR has a potential for recurrence and chronicity, with subsequent risk of permanent visual impairment. Various treatment modalities have been tried in the past, with variable results. The fact remains that unless the risk factors predisposing to the disease are appropriately addressed, the management may be inadequate.

In the present-day scenario, in which rising levels of psychological stress are being implicated in the etiopathogenesis of a variety of diseases, stress management is the need of the hour. Therapeutic strategies for CSCR should target measures to relieve stress and equip the affected individuals to effectively manage stress. Adequate long term follow up and continued provision of holistic care are also important in the management of these patients.

LIMITATIONS OF THE STUDY

- We did not do ICG angiography for our study patients. Therefore, we have not studied choroidal vascular hyperpermeability in the eyes of these patients.
- Although the possibility of intra-observer variability in the manual measurement of sub foveal choroidal thickness was taken into account during the design of the study, and measures to address this issue were taken, it is likely that, in spite of this, some intra-observer variability would have remained.
- This was a cross sectional study, with a single point of contact with each study patient, when the assessment of stress scores and choroidal thickness was done. This would not have been able to capture the variation in stress levels and choroidal thickness, and their effect on the evolution of the pathophysiological changes of the disease.

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APPENDIX 1: IRB APPROVAL FORM

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

March 09, 2018

Dr. Reshmi Mathews,
PG Registrar,
Department of Ophthalmology,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant: New Proposal:**
Role of choroidal thickness and psychological stress in Central serous – chorioretinopathy.
Dr. Reshmi Mathews (Emp. No. 21433), PG Registrar, Ophthalmology, Dr. Sheeja Susan John (Emp. No. 31049), Ophthalmology, Dr. Saban Horo (Emp. No. 31178) Ophthalmology, Mrs. Grace Rebekah J (Emp. No. 32070), Biostatistics.

Ref: IRB Min. No. 11094 [OBSERVE] dated 10.01.2018

Dear Dr. Reshmi Mathews,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Sheeja Susan John, Dept. of Ophthalmology, CMC, Vellore

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

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Ref: IRB Min. No. 11094 [OBSERVE] dated 10.01.2018

Dear Dr. Reshmi Mathews,

The Institutional Review Board **(Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Role of choroidal thickness and psychological stress in Central serous – chorioretinopathy" on January 10th 2018.

The Committee reviewed the following documents:

1. IRB application format
2. Signature Pages
3. Consent Form Information Sheet, Child Assent Forms (English, Tamil, Hindi)
4. Cvs of Drs. Sheeja, Saban Horo, Reshmi, Grace.
5. No. of documents 1- 4.

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on January 10th 2018 in the BRTC Conference Hall, Biostatistics Building, Christian Medical College, Vellore 632 004.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. RekhaPai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist &Epidemiologist
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr Sneha Varkki	MBBS, DCH, DNB	Professor, Paediatrics, CMC, Vellore	Internal, Clinician
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Asha Solomon	MSc Nursing	Associate Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse

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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Dr. Santhanam Sridhar	MBBS, DCH, DNB	Professor, Neonatology, CMC, Vellore	Internal, Clinician
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician
Dr. Shyam Kumar NK	MBBS, DMRD, DNB, FRCR, FRANZCR	Professor, Radiology, CMC, Vellore	Internal, Clinician
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. John Antony Jude Prakash	MBBS, MD	Professor, Clinical Microbiology, CMC, Vellore.	Internal, Clinician.
Dr. Ajith Sivadasan	MD, DM	Professor, Neurological Sciences, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of Withdrawals for the study entitled: "Role of choroidal thickness and psychological stress in Central serous – chorioretinopathy" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of 62,280/- INR (Rupees Sixty Two Thousand Two Hundred Only) will be granted for 18 Months.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

IRB Min. No. 11094 [OBSERVE] dated 10.01.2018

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

APPENDIX 2: INFORMATION SHEET AND CONSENT FORMS

Protocol No:

Role of choroidal thickness and psychological stress in Central serous chorioretinopathy

Information Sheet –Group 1

Name of participant:

You are invited to take part in this study. The information in this document is meant to help you decide whether or not to take part in the study. Please feel free to ask if you have any queries or concerns.

What is the study about?

Central serous chorioretinopathy (CSCR) is a disease affecting the choroid and retina – the vascular and nervous layers of the eyeball. In CSCR, there is fluid accumulation in the central part of the retina, resulting in decreased vision. Many risk factors have been implicated in the causation of CSCR. Psychological stress is one of the major risk factors that have been studied. In recent years, it has been shown, with the help of the newer OCT scan systems, that the choroidal thickness or thickness of the choroid (the vascular layer of the eyeball) is increased in patients with CSCR. There have been no studies so far, that have looked at the relationship between choroidal thickness and psychological stress in patients with CSCR.

In this study, we will measure the choroidal thickness of the eye (using OCT scan), and the level of psychological stress (using a questionnaire), both in patients with CSCR (Group 1), and in people who do not have CSCR (Group 2). We will also study the relationship between choroidal thickness and psychological stress in the study subjects.

If you take part, what will you have to do?

If you take part in the study, you will have a routine eye examination. Other routine eye tests like OCT scan of your eye, and fundus fluorescein angiography, which are needed for the diagnosis and treatment of your eye disease, will be done. You will also be administered a questionnaire to assess your stress levels, along with measurement of blood pressure, and optical biometry (a test used to measure the length of your eyeball).

Are there any risks for you if you take part in the study?

In addition to the routine eye examination and tests required for the management of your eye disease, participation in the study only involves an additional test used to measure the length of your eyeball (optical biometry).You will also be administered a questionnaire to assess your stress levels.

We do not expect any injury to happen to you as a result of participation in this study; but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. However, we are unable to provide any monetary compensation.

Do you have to pay?

You will have to pay only for the tests that are required for the routine treatment of your eye disease. All additional investigations for the study will be done free of cost.

What are the benefits to you if you take part in the study?

If you participate in the study,

1. You will be screened for the risk factors, which may have played a role in the development of your eye disease.
2. In case you are found to have any of these risk factors, you will be referred to specialist doctors for further evaluation and appropriate management.
3. Addressing the risk factors will help in better management of the eye problem in terms of faster disease control and prevention of recurrence.
3. Early detection and treatment of such risk factors will also help in preventing systemic diseases such as heart attack and stroke.

What are the possible benefits to other people?

The results of this study may provide benefits to the society in terms of advancement of medical knowledge, disease prevention and therapeutic benefit to future patients. We hope that this study will help us to understand this disease better. In the future, this may help us to devise strategies to prevent or delay the development of this eye disease in at-risk patients, as well as to prevent the occurrence of systemic complications like heart attack and stroke.

Can you decide not to participate?

Your participation in this study is entirely voluntary, and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way. Your doctor will still take care of you, and you will not lose any benefits to which you are entitled.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal, but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, you may contact Dr. Reshmi Mathews or Dr.Sheeja Susan John or Dr.Saban Horo(Tel: 0416 2281201) or email: reshmimathews19@gmail.com

Protocol No:

Role of choroidal thickness and psychological stress in Central serous chorioretinopathy

Information Sheet –Group 2

Name of participant:

You are invited to take part in this study. The information in this document is meant to help you decide whether or not to take part in the study. Please feel free to ask if you have any queries or concerns.

What is the study about?

Central serous chorioretinopathy (CSCR) is a disease affecting the choroid and retina – the vascular and nervous layers of the eyeball. In CSCR, there is fluid accumulation in the central part of the retina, resulting in decreased vision. Many risk factors have been implicated in the causation of CSCR. Psychological stress is one of the major risk factors that have been studied. In recent years, it has been shown, with the help of the newer OCT scan systems, that the choroidal thickness or thickness of the choroid (the vascular layer of the eyeball) is increased in patients with CSCR. There have been no studies so far, that have looked at the relationship between choroidal thickness and psychological stress in patients with CSCR.

In this study, we will measure the choroidal thickness of the eye (using OCT scan), and the level of psychological stress (using a questionnaire), both in patients with CSCR (Group 1), and in people who do not have CSCR (Group 2). We will also study the relationship between choroidal thickness and psychological stress in the study subjects.

If you take part, what will you have to do?

If you take part in the study, you will have a routine eye examination. You will be administered a questionnaire to assess your stress levels. You will also have an OCT scan of your eye, and optical biometry (a test used to measure the length of your eyeball),and measurement of your blood pressure.

Are there any risks for you if you take part in the study?

In addition to a routine eye examination, participation in the study only involves an OCT scan of your eye, and optical biometry (a test used to measure the length of your eyeball),and measurement of your blood pressure. You will also be administered a questionnaire to assess your stress levels. All the tests done in the study are non-invasive, and we do not expect any injury to happen to you as a result of participation in this study; but if you do develop any side effects or problems due to the study, these will be treated at no cost to you. However, we are unable to provide any monetary compensation.

Do you have to pay?

You will have to pay only for the tests and investigations, which are required for the routine treatment of your eye condition. All additional investigations done for the study will be done free of cost.

What are the benefits to you if you take part in the study?
If you participate in the study,
1. You will be screened for all the potential risk factors for CSCR.
2. In case you are found to have any of these risk factors, such as high blood pressure or high levels of psychological stress, you will be referred to specialist doctors for further evaluation and appropriate management.
3. Early detection and treatment of such risk factors will also help in preventing systemic diseases, such as heart attack and stroke.

What are the possible benefits to other people?
The results of this study may provide benefits to the society in terms of advancement of medical knowledge, disease prevention and therapeutic benefit to future patients. We hope that this study will help us to understand this disease better. In the future, this may help us to devise strategies to prevent or delay the development of this eye disease in at-risk patients, as well as to prevent the occurrence of systemic complications like heart attack and stroke.

Can you decide not to participate?
Your participation in this study is entirely voluntary, and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way. Your doctor will still take care of you, and you will not lose any benefits to which you are entitled.

Will your personal details be kept confidential?
The results of this study may be published in a medical journal, but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, you may contact Dr. Reshmi Mathews or Dr.Sheeja Susan John or Dr.Saban Horo(Tel: 0416 2281201) or email: reshmimathews19@gmail.com

सेन्ट्रल सीरज कोरियो रेटिनीपथी में कोरोइड़ और मनोवैज्ञानिक तानाव का जाँच

सूचना पत्र–समूह 1

जाँच में भाग लेने वाले का नामः

इस जाँच में भाग लेने के लिए आपको आमंत्रण है। इस सूचना को पढ़कर आप जाँच में भाग लेने के बारे में विचार कर सकते हैं। इस विषय में आपको कोई सवाल या जानकारी पूछना है, तो आप पूछ सकते हैं।

- यह जाँच किस विषय संबंधित है?

  सेन्ट्रल सीरज कोरिया रेटिनोपथी (सी.**एस**.सी.आर) आँख के रेटिना (आँख का नस वाला परत) और कोरोइड़ (आँख का रक्त संवहिनी वाला परत) की बीमारी है। इस बीमारी में रेटिना के मध्य विभाग में पानी इकट्ठा होता है जिसके कारण आँख की रोशनी कम हो जाती है।

  इस बीमारी के अनेक कारण हैं, जिनमें से सबसे महत्वपूर्ण कारण हैं, मनौवैज्ञानिक तनाव–जिसके विषय में काफी पढ़ाई हुई है। पिछले कुछ वर्षों में ओ.सी.टी. स्केन के आने के बाद पता चला है कि इन मरीजों में कोरोइड (आँख का रक्त संवहिनी वाला परत) की मोटाई ज्यादा होती है। मगर आज तक कोई ऐसा अनुसंधान नहीं हुआ है जिसमें कोरोइड की मोटाई और मनोवैज्ञानिक तनाव के बीच के संबंध का पढ़ाई हुई हो।

  इस जाँच में हम कोरोइड की मोटाई का नाप करेंगे (ओ.सी.टी. स्केन के द्वारा), और मनोवैज्ञानिक तनाव का नाप करेंगे (एक प्रश्नावली के द्वारा)। यह जाँच दोनों समूह वाले मरीजों में किए जाएँगे– जिनमें सी0एस0सी0आर0 हैं (पहला समूह), और जिनमें सी0एस0सी0आर0 नहीं है (दूसरा समूह)।

  मनोवैज्ञानिक तनाव और कोरोइड की मोटाई के बीच के संबंध का जाँच भी किया जाएगा।

- इस जाँच में भाग लेंगे, जो आपको क्या करना होगा?

  अगर आप इस जाँच में भाग लेंगे तो आपकी आँखों का संपूर्ण परीक्षण किया जाएगा। अन्य जाँच जैसे ओ0सी0टी0 स्केन और फण्डस फ्लूरसीन एन्जियोग्रेफी (**एफ.एफ.ए**) आपके बीमारी के लिए जरूरी जाँच हैं, यह भी किए जाएँगे। आपके मनोवैज्ञानिक तनाव की जानकारी प्राप्त करने के लिए एक प्रश्नावली भी दिया जाएगा। इसके अलावा आपका रक्त चाप का नाप किया जाएगा। और साथ में ओप्टिकल बाइओमेट्री (आँखों की लंबाई का जाँच) भी किया जाएगा।

- इस जाँच में भाग लेने से क्या आपको कोई परेशानी उत्पन्न हो सकती है?

  इस जाँच में भाग लेने से आपकी बीमारी हेतु सामान्य जाँच के अलावा एक और जाँच किया जाएगा, ओप्टिकल बाइओमेट्री (जिसमें आँखों की लंबाई का जाँच किया जाता है)। साथ में मनोवैज्ञानिक तनाव नापने के लिए एक प्रश्नावली भी दी जाएगी। इस जाँच में भाग लेने से आपको कोई परेशानी नहीं होनी चाहिए। परंतु स्वास्थ्य विषयक कोई परेशानी अथवा अन्य परिणाम दिखाई दें, तो आपको मुफ्त उपचार किया जाएगा। मगर द्रव्य रूप में आपको कोई हर्जाना नहीं दिया जाएगा।

- क्या आपको जाँच के लिए कुछ अदा करना पड़ेगा?

  इस जाँच में आपकी आँखों के नियमित उपचारों के लिए जो सर्वसाधारण परीक्षण हैं, उनके लिए आपको कुछ रकम भरने होंगे। इनके सिवाय अधिक जानकारी प्राप्त करने के लिए जो परीक्षण किए जाएंगे, वह मुफ्त है

- इस जाँच में भाग लेने से आपका क्या लाभ है?

  1. इस जाँच में भाग लेने से जिन कारणों के दौरान आपको यह बीमारी हुई है, उनके पूरे जाँच किए जाएंगे।
  2. अगर ऐसे कारणों में से कुछ आप में पाया गया, तो उनके इलाज के लिए विशेषज्ञों के पास आपको भेजा जाएगा।
  3. समय पर उचित इलाज करने से आपकी बीमारी का हल जल्दी हो सकता है।
  4. ऐसे कारणों का पहले से उचित इलाज करेंगे तो आगे चलकर भयंकर रोग जैसे कि हृदय रोग, रक्तवाहिनी का फटना, आदि से आप बच सकते हैं।

- इस जाँच से अन्य लोगों को क्या फायदा है?

  इस शोधकार्य से वैधकीय ज्ञान में वृद्धि होगी, रोगों से बचाव तथा उनके उपचारों की जानकारी प्राप्त होंगी। जिससे भविष्य में समाज को, अर्थात रोगों से पीढ़ित लोगों को अवश्य लाभ होगा। यहाँ तक कि उचित इलाज से हृदय रोग और रक्तवाहिनी फटने जैसे भयंकर बीमारियों से भी बचाव हो सकता है।

- क्या आप इस जाँच में भाग न लेने का निर्णय ले सकते हैं?

  इस जाँच में आप स्वेच्छा भाग ले सकते हैं और स्वेच्छा आपकी अनुमति वापिस भी ले सकते हैं। आपके जाँच में सम्मिलित न होने पर भी अस्पताल द्वारा आपके उपचारों पर कोई परिणाम नहीं होगा। आपके डॉक्टर्स आपका बराबर ध्यान देंगे और जो सुविधाएं आपको मिलनी चाहिए, वो भी बराबर मिलेंगी।

- क्या आपकी व्यक्तिगत जानकारी गुप्त रखी जाएंगी?

  इस जाँच से जो नतीजे निकलेंगे, ये वैज्ञानिक पत्रिकाओं में प्रकाशित किए जाएंगे। प्रकाशन तथा प्रस्तुतीकरण में आपकी पहचान छुपायी जाएगी। परंतु इस विषय से संबंधित लोगों को अभ्यास हेतु इसकी जानकारी आपकी अनुमति बिना दी जाएगी। अगर आपको कोई सवाल पूछना है तो आप डॉ रेश्मि मॉथ्यूज, डॉ शीजा सुसान जॉन, डॉ सबन होरो इनसे संपर्क कर सकते हैं।

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सेन्ट्रल सीरज कोरिया रेटिनोपैथी में कोरोइड़ और मनोवैज्ञानिक तनाव का जाँच

सूचना पत्र– समूह 2

जाँच में भाग लेने वाले का नामः

इस जाँच में भाग लेने के लिए आपको आमंत्रण है। इस सूचना को पढ़कर आप जाँच भाग लेने के बारे में विचार कर सकते हैं। इस विषय में आपको कोई सवाल या जानकारी पूछना है, तो आप पूछ सकते हैं।

- यह जाँच किस विषय संबंधित है?

  सेन्ट्रल सीरज कोरिया रेटिनोपंथी (सी.एस.सी.आर.) आँख के रेटिना (आँख का नस वाला परत) और कोरोइड (आँख का रक्त संवहिनी वाला परत) की बीमारी है। इस बीमारी में रेटिना के मध्य विभाग में पानी इकट्ठा होता है, जिसके कारण आँख की रोशनी कम हो जाती है।

  इस बीमारी के अनेक कारण हैं, जिनमें से सबसे महत्वपूर्ण कारण हैं, मनोवैज्ञानिक तनाव–जिसके विषय में काफी पढ़ाई हुई है पिछले कुछ वर्षों में ओ.सी.टी. स्केन के आने के बाद पता चला है कि इन मरीजों में कोरोइड़ (आँख का रक्त संवहिनी वाला परत) की मोटाई ज्यादा होती है। मगर आज तक कोई ऐसा अनुसंधान नहीं हुआ है जिसमें कोरोइड़ की मोटाई और मनोवैज्ञानिक तनाव के संबंध में पढ़ाई हुई हो।

  इस जाँच में हम कोरोइड़ की मोटाई का नाप करेंगे (ओ.सी.टी. स्केन के द्वारा), और मनोवैज्ञानिक तनाव नाप करेंगे (एक प्रश्नावली के द्वारा) यह जाँच दोनों समूह वाले मरीजों में किए जाएँगे–जिनमें सी.एस.सी.आर. है (पहला समूह) और जिनमें सी.एस.सी.आर. नहीं है (दूसरा समूह)।

  मनोवैज्ञानिक तनाव और कोरोइड़ की मोटाई के बीच के संबंध का जाँच भी किया जाएगा।

- इस जाँच में भाग लेंगे तो आपको क्या करना होगा?

  अगर आप इस जाँच में भाग लेंगे तो आपकी आँखों का संपूर्ण परीक्षण किया जाएगा। आपके मनोवैज्ञानिक तनाव की जानकारी प्राप्त करने के लिए एक प्रश्नावली भी दिया जाएगा। इसके अलावा आपकी आँख का ओ.सी.टी. स्केन और ओप्टिकल बाइओमेट्री (आँखों की लंबाई का जाँच) जाँच भी होगा। साथ में आपका रक्त चाप भी नापा जाएगा।

- इस जाँच में भाग लेने से क्या आपको कोई परेशानी उत्पन्न हो सकते हैं?

  इस जाँच में भाग लेने से आपकी बीमारी हेतु सामान्य जाँच के अलावा ओ.सी. टी. स्केन और ओप्टिकल बाइओमेट्री (आँखों की लंबाई का जाँच) किया जाएगा। साथ में रक्त चाप भी नापा जाएगा और मनोवैज्ञानिक तनाव नापने के लिए एक प्रश्नावली भी दी जाएगी। इस जाँच में भाग लेने से आपको कोई

परेशानी नहीं होनी चाहिए। परंतु स्वास्थ्य विषयक कोई परेशानी अथवा अन्य परिणाम दिखाई दें, तो आपको मुफ्त उपचार किया जाएगा। मगर द्रव्य रूप में आपको कोई हर्जाना नहीं दिया जाएगा।

- क्या आपको जाँच के लिए कुछ अदा करना पड़ेगा?

  इस जाँच में आपकी आँखों के नियमित उपचारों के लिए जो सर्वसाधारण परीक्षण हैं, उनके लिए आपको कुछ रकम भरने होंगे। इनके सिवाय अधिक जानकारी प्राप्त करने के लिए जो परीक्षण किए जाएंगे, वह मुफ्त हैं।

- इस जाँच में भाग लेने से आपका क्या लाभ है?

  इस जाँच में भाग लेने से –

  1. जिन कारणों से सी.एस.सी.आर. होता है, उनका पूरा जाँच किया जाएगा।
  2. अगर आप में ऐसे कुछ कारण पाया गया जैसे कि अधिक रक्त चाप, अधिक मनोवैज्ञानिक तनाव आदि, उनके इलाज के लिए विशेषज्ञों के पास आपको भेजा जाएगा।
  3. ऐसे कारणों का पहले से उचित इलाज करेंगे तो आगे चल कर भयंकर रोग जैसे कि हृदयरोग, रक्तवाहिनी का फटना, आदि से आप बच सकते हैं।

- इस जाँच से अन्य लोगों को क्या फायदा है?

  इस शोधकार्य से वैधकीय ज्ञान में वृद्धि होगी, रोगों से बचाव तथा उनके उपचारों की जानकारी प्राप्त होंगी। जिससे भविष्य में समाज को, अर्थात् रोगों से पीड़ित लोगों को अवश्य लाभ होगा। यहाँ तक कि उचित इलाज से हृदय रोग और रक्तवाहिनी फटने जैसे भयंकर बीमारियों से भी बचाव हो सकता है।

- क्या आप इस जाँच में भाग न लेने का निर्णय ले सकते हैं?

  इस जाँच में आप स्वेच्छा भाग ले सकते हैं और स्वेच्छा आपकी अनुमती वापिस भी ले सकते हैं। आपके जाँच में सम्मिलित न होने पर भी अस्पताल द्वारा आपके उपचारों पर कोई परिणाम नहीं होगा। आपके डॉक्टर्स आपका बराबर ध्यान रखेंगे, और जो सुविधाएँ आपको मिलनी चाहिए, वो भी बराबर मिलेंगी।

- क्या आपकी व्यक्तिगत जानकारी गुप्त रखी जाएंगी?

  इस जाँच से जो नतीजे निकलेंगे, ये वैज्ञानिक पत्रिकाओं में प्रकाशित किए जाएंगे। प्रकाशन या प्रस्तुतीकरण में आपकी पहचान छुपाई जाएंगी। परंतु इस विषय से संबंधित लोगों को अभयास हेतु इसकी जानकारी आपकी अनुमति के बिना दी जाएगी।

  अगर आपको कोई सवाल पूछना है तो आप डॉ रेश्मि मॉथ्यूज, डॉ शीजा सुसान जॉन, डॉ सबन होरो, इनसे संपर्क कर सकते हैं।

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சென்ட்ரல் செரோஸ் கொரியோரெட்டினாபதியில் கொராய்டலின் தடிமண் மற்றும் உளவியல் மன அழுத்ததின் பங்கு

தகவல் தாள் (குழு -1)

ஆய்வில் பங்கு பெறுபவருக்கான தகவல் தாள்

பங்கேற்பவரின் பெயர்:.....

உங்களை இந்த ஆய்வில் பங்கு பெற அழைக்கிறோம் இந்த தாளில் உள்ள தகவல்களை நீங்கள் படித்தறிந்த பின் இந்த ஆய்வில் பங்கு பெறலமா வேண்டாமா என்று நீங்கள் முடிவு செய்யலாம். இது தொடர்பான கேள்விகள் மற்றும் சந்தேகங்களை நீங்கள் எங்களிடம் தயக்கமின்றி தெரிவிக்கலாம்.

இந்த ஆய்வு எதைப் பற்றியது:-

கண் விழியில் உள்ள விழிநடுப்படலம், மற்றும் விழித்திரையில் இரத்தம் சுமந்து செல்லும் நாளம் மற்றும் நரம்பு அடுக்கில் ஏற்படும் நோய் சென்ட்ரல் செரோஸ் கொரியோரெட்டினாபதி (CSCR) ஆகும்.

சென்ட்ரல் செரோஸ் கோரியோ ரெட்டினாபதி (CSCR) என்பது விழித்திரை மையப்பகுதியில் திரவ குவிப்பு ஏற்படுகிறது. இதன் விளைவாக குறைந்த பார்வை ஏற்படுகிறது. சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி காரணமாக பல ஆபத்து காரணிகள் தொடர்பு படுத்தப்பட்டுள்ளன. உளவியல் ரீதியான மன அழுத்தம் முக்கிய ஆய்வுக் காரணிகளில் ஒன்றாகும். சமீபத்திய காலங்களில், இது புதிய ஒசி.ீடி(OCT) ஸ்கேன் முறைகளின் உதவியுடன் சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி (CSCR) உடைய நோயாளிகளிடமிருந்து அதிகப்படியான கொராய்டு அல்லது தடிமன் (கண்விழியில் குருதியை எடுத்துச் செல்லும் நாளங்கள் அடுக்கு) அதிகரித்துள்ளது. சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி உடைய நோயாளிகளுக்கு உடற்கூறியல் தடிமன் மற்றும் உளவியல் மன அழுத்தம்

ஆகியவற்றிற்கு இடையே உள்ள உறவை பற்றிய எந்த ஆய்வும் இதுவரை மேற்கொள்ளப்படவில்லை.

இந்த ஆய்வில் கொராய்டல் தடிமன் மற்றும் உளவியல் அழுத்தம் ஆகியவற்றிற்கும் இடையேயான உறவை சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி (குழு-1) நபர்கள் பத்திலும் (குழு-2) ஓசி.டி (OCT) ஸ்கேன் பயன்படுத்தியும், கொராய்டல் தடிமன் அளவும் ஒரு கேள்வித் தாளை பயன்படுத்தி உளவியல் அழுத்தத்தின் அளவும் ஆராய்வோம்.

இந்த ஆய்வில் பங்கேற்க, நீங்கள் என்ன செய்ய வேண்டும்:

இந்த ஆய்வில் பங்கேற்க நீங்கள் ஒரு கண் பரிசோதனை செய்ய வேண்டும். மற்ற வழக்கமான கண் பரிசோதனைகளாகிய ஓசி.டி(OCT) ஸ்கேன் மற்றும் .பன்டஸ் ப்ளோரசீன் ஆஞ்சியோகிரா.பி பயன்படுத்தி உங்கள் கண் நோய் கண்டறிதல் மற்றும் சிகிச்சைக்கு உட்படுத்தபடுவீர்கள். இரத்த அழுத்த அளவைக் கொண்டு உங்கள் அழுத்த அளவீடுகள் மற்றும் (கண் விழியின் நீளத்தை அளவிட ஒரு சோதனை) அளவீடுகளை மதிப்பீடு செய்ய ஒரு கேள்வித்தாள் மூலம் அறியப்படும்.

இந்த ஆய்வில் பங்கு பெறுவதால் உங்களுக்கு ஏதாவது ஆபத்து உள்ளதா?

இந்த ஆய்வில் பங்கேற்பதன் விளைவாக உங்களுக்கு எந்த காயமும் ஏற்படாது என்று நாங்கள் எதிர்பார்க்கிறோம். இந்த ஆய்வினால் ஏதாவது பக்க விளைவுகளோ அல்லது சிக்கல்கள் ஏற்பட்டால் உங்களுக்கு இலவசமாக சிகிச்சை அளிக்கப்படும் ஆனால் எந்தவொரு பண இழப்பீடும் வழங்க முடியாது.

நீங்கள் பணம் ஏதும் செலுத்த வேண்டுமா?

உங்கள் கண் நோய்க்கு வழக்கமான சிகிச்சை தேவைப்படும்

பரிசோதனைகளுக்கு மட்டும் பணம் செலுத்த வேண்டும். ஆய்விற்கான கூடுதல் பரிசோதனைகளுக்கு சிகிச்சை இலவசமாக அளிக்கப்படும்.

ஆய்வில் பங்கேற்பதால் என்ன நன்மைகள் நீங்கள் பெற முடியும்:

நீங்கள் ஆய்வில் பங்கேற்பதால்

1. உங்கள் கண் நோய்க்கான வளர்ச்சியில் ஆபத்து காரணிகளுக்கு நீங்கள் ஆய்வுக்கு உட்படுத்தப்படுவதில் பங்கு பெறுகிறீர்கள்.

2. இந்த ஆபத்து காரணிகளை ஏதேனும் இருப்பதாக கண்டறியப்பட்டால், சிறப்பு மருத்துவர்களால் பரிந்துரை செய்யபட்டு பொருத்தமான நிர்வாகம் நடைபெற உதவியாய் இருப்பீர்கள்.

3. ஆபத்துக்கான காரணிகள் அறிந்து கொள்வதால் விரைவான நோய் கட்டுபாடு, மற்றும் மீண்டும் பிரச்சனையை தடுத்தல் ஆகியவற்றின் அடிப்படையில் கண் பிரச்சனைகளுக்கு சிறந்த மேலாண்மைக்கு வழிவகுக்கும்.

4. ஆரம்பத்திலேயே நோய்கள் ஆபத்துத் தன்மைகளை கண்டறிவது மற்றும் சிகிச்சை அளித்தல் மூலம் இதய பாதிப்பு மற்றும் பக்கவாதம் போன்ற அமைப்புமுறை நோய்களை தடுப்பதில் முக்கிய பங்குளிப்பாகும்.

மற்றவர்களுக்கு சாத்தியமான நன்மைகள் யாவை

மருத்துவ ஆய்வு, நோய் தடுப்பு மற்றும் வருங்கால நோயாளிக்கு சிகிச்சை அளித்தல் ஆகியவற்றின் முன்னேற்றத்தின் அடிப்படையில் இந்த ஆய்வின் முடிவுகள் சமூகத்திற்கு நன்மைகள் வழங்கலாம்.

எதிர் காலத்தில் இந்த ஆபத்து (CSCR) நோய்களுக்கு இந்த கண் நோயை தடுக்க அல்லது தாமதப்படுத்தல் மற்றும் இதயத் தாக்குதல் மற்றும் பக்கவாதம் போன்ற முறை சார்ந்த சிக்கல்களை

ஏற்படாமல் தடுக்க வேண்டிய உத்திகளை திட்டமிட உதவும் என்றும் இந்த நோயை புரிந்து கொள்வதற்கு இந்த ஆய்வு நமக்கு உதவும் என்று நாங்கள் நம்புகிறோம்.

இந்த ஆய்வில் நீங்கள் கட்டாயம் பங்கு பெற வேண்டுமா?

இந்த ஆய்வில் பங்கு பெற உங்களுக்கு எந்த வித கட்டாயமோ, வற்புறுத்தலோ கிடையாது. உங்கள் முழு விருப்பத்தின் பேரில் மட்டுமே நீங்கள் இந்த ஆய்வில் பங்கு பெற அழைக்கப்படுகிறீர்கள். ஒரு வேளை உங்களுக்கு இந்த ஆய்வில் பங்குபெற விருப்பம் இல்லாவிட்டால், நீங்கள் இந்த ஆய்வில் இருந்து விலகிக் கொள்ளலாம். நீங்கள் அவ்வாறு விலகிக் கொண்டால், அது உங்கள் கண் நோய்க்கு இந்த மருத்துவமனையில் அளிக்கப்படும் சிகிச்சை எந்த விதத்திலும் பாதிக்காது.

உங்கள் தனிப்பட்ட விவரங்கள் நம்பகமான முறையில் பாதுகாக்கப்படுமா?

இந்த ஆய்வின் முடிவுகள் மருத்துவ பத்திரிக்கைகளில் வெளியிடப்படலாம். ஆனால் உங்கள் பெயரோ தனிப்பட்ட விவரமோ எந்த விதத்திலும் வெளியிடப்படமாட்டாது எனினும், இந்த ஆய்வில் நீங்கள் பங்கு பெற்றால் உங்கள் மருத்துவ விவரங்கள் உங்கள் அனுமதியின்றி, ஆய்வு தொடர்பான அதிகரிகளால் மதிப்பாய்வு செய்யப்படும்.

உங்களுக்கு மேலும் ஏதேனும் சந்தேகங்கள் இருந்தால் நீங்கள் Dr. ரேஷ்மி மேத்யூ அல்லது Dr. ஷீஜா சூசன் ஜான் அல்லது Dr. சபன் ஹோரோ ஆகியோரை தெலைபேசி எண்: 0416-2281201 தொடர்பு கொள்ளலாம்.

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தகவல் தாள் (குழு -2)

ஆய்வில் பங்கு பெறுபவருக்கான தகவல் தாள்

பங்கேற்பவரின் பெயர்:.....

உங்களை இந்த ஆய்வில் பங்கு பெற அழைக்கிறோம் இந்த தாளில் உள்ள தகவல்களை நீங்கள் படித்தறிந்த பின் இந்த ஆய்வில் பங்கு பெறலமா வேண்டாமா என்று நீங்கள் முடிவு செய்யலாம். இது தொடர்பான கேள்விகள் மற்றும் சந்தேகங்களை நீங்கள் எங்களிடம் தயக்கமின்றி தெரிவிக்கலாம்.

இந்த ஆய்வு எதைப் பற்றியது:-

கண் விழியில் உள்ள விழிநடுப்படலம், மற்றும் விழித்திரையில் இரத்தம் சுமந்து செல்லும் நாளம் மற்றும் நரம்பு அடுக்கில் ஏற்படும் நோய் சென்ட்ரல் செரோஸ் கொரியோரெட்டினாபதி (CSCR) ஆகும்.

சென்ட்ரல் செரோஸ் கோரியோ ரெட்டினாபதி (CSCR) என்பது விழித்திரை மையப்பகுதியில் திரவ குவிப்பு ஏற்படுகிறது. இதன் விளைவாக குறைந்த பார்வை ஏற்படுகிறது. சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி காரணமாக பல ஆபத்து காரணிகள் தொடர்பு படுத்தப்பட்டுள்ளன. உளவியல் ரீதியான மன அழுத்தம் முக்கிய ஆய்வுக் காரணிகளில் ஒன்றாகும். சமீபத்திய காலங்களில், இது புதிய ஒசி.ட்டி(OCT) ஸ்கேன் முறைகளின் உதவியுடன் சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி (CSCR) உடைய நோயாளிகளிடமிருந்து அதிகப்படியான கொராய்டு அல்லது தடிமன் (கண்விழியில் குருதியை எடுத்துச் செல்லும் நாளங்கள் அடுக்கு) அதிகரித்துள்ளது. சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி உடைய நோயாளிகளுக்கு உடற்கூறியல் தடிமன் மற்றும் உளவியல் மன அழுத்தம்

ஆகியவற்றிற்கு இடையே உள்ள உறவை பற்றிய எந்த ஆய்வும் இதுவரை மேற்கொள்ளப்படவில்லை.

இந்த ஆய்வில் கொராய்டல் தடிமன் மற்றும் உளவியல் அழுத்தம் ஆகியவற்றிற்கும் இடையேயான உறவை சென்ட்ரல் செரோஸ் கொரியோ ரெட்டினாபதி (குழு-1) நபர்கள் பத்திலும் (குழு-2) ஒசி.ட்டி (OCT) ஸ்கேன் பயன்படுத்தியும், கொராய்டல் தடிமன் அளவும் ஒரு கேள்வித் தாளை பயன்படுத்தி உளவியல் அழுத்தத்தின் அளவும் ஆராய்வோம்.

இந்த ஆய்வில் பங்கேற்க, நீங்கள் என்ன செய்ய வேண்டும்:

இந்த ஆய்வில் பங்கேற்க நீங்கள் ஒரு கண் பரிசோதனை செய்ய வேண்டும். மற்ற வழக்கமான கண் பரிசோதனைகளாகிய ஒசி.ட்டி(OCT) ஸ்கேன் மற்றும் .ட்பன்டஸ் ப்ளோரசீன் ஆஞ்சியோகிரா.ட்பி பயன்படுத்தி உங்கள் கண் நோய் கண்டறிதல் மற்றும் சிகிச்சைக்கு உட்படுத்தபடுவீர்கள். இரத்த அழுத்த அளவைக் கொண்டு உங்கள் அழுத்த அளவீடுகள் மற்றும் (கண் விழியின் நீளத்தை அளவிட ஒரு சோதனை) அளவீடுகளை மதிப்பீடு செய்ய ஒரு கேள்வித்தாள் மூலம் அறியப்படும்.

இந்த ஆய்வில் பங்கு பெறுவதால் உங்களுக்கு ஏதாவது ஆபத்து உள்ளதா?

இந்த ஆய்வில் பங்கேற்பதன் விளைவாக உங்களுக்கு எந்த காயமும் ஏற்படாது என்று நாங்கள் எதிர்பார்க்கிறோம். இந்த ஆய்வினால் ஏதாவது பக்க விளைவுகளோ அல்லது சிக்கல்கள் ஏற்பட்டால் உங்களுக்கு இலவசமாக சிகிச்சை அளிக்கப்படும் ஆனால் எந்தவொரு பண இழப்பீடும் வழங்க முடியாது.

நீங்கள் பணம் ஏதும் செலுத்த வேண்டுமா?

உங்கள் கண் நோய்க்கு வழக்கமான சிகிச்சை தேவைப்படும்

பரிசோதனைகளுக்கு மட்டும் பணம் செலுத்த வேண்டும். ஆய்விற்கான கூடுதல் பரிசோதனைகளுக்கு சிகிச்சை இலவசமாக அளிக்கப்படும்.

ஆய்வில் பங்கேற்பதால் என்ன நன்மைகள் நீங்கள் பெற முடியும்:

நீங்கள் ஆய்வில் பங்கேற்பதால்

1. உங்கள் கண் நோய்க்கான வளர்ச்சியில் ஆபத்து காரணிகளுக்கு நீங்கள் ஆய்வுக்கு உட்படுத்தப்படுவதில் பங்கு பெறுகிறீர்கள்.

2. இந்த ஆபத்து காரணிகளை ஏதேனும் இருப்பதாக கண்டறியப்பட்டால், சிறப்பு மருத்துவர்களால் பரிந்துரை செய்யபட்டு பொருத்தமான நிர்வாகம் நடைபெற உதவியாய் இருப்பீர்கள்.

3. ஆரம்பத்திலேயே நோய்கள் ஆபத்துத் தன்மைகளை கண்டறிவது மற்றும் சிகிச்சை அளித்தல் மூலம் இதய பாதிப்பு மற்றும் பக்கவாதம் போன்ற அமைப்புமுறை நோய்களை தடுப்பதில் முக்கிய பங்குளிப்பாகும்.

மற்றவர்களுக்கு சாத்தியமான நன்மைகள் யாவை

மருத்துவ ஆய்வு, நோய் தடுப்பு மற்றும் வருங்கால நோயாளிக்கு சிகிச்சை அளித்தல் ஆகியவற்றின் முன்னேற்றத்தின் அடிப்படையில் இந்த ஆய்வின் முடிவுகள் சமூகத்திற்கு நன்மைகள் வழங்கலாம்.

எதிர் காலத்தில் இந்த ஆபத்து (CSCR) நோய்களுக்கு இந்த கண் நோயை தடுக்க அல்லது தாமதப்படுத்தல் மற்றும் இதயத் தாக்குதல் மற்றும் பக்கவாதம் போன்ற முறை சார்ந்த சிக்கல்களை ஏற்படாமல் தடுக்க வேண்டிய உத்திகளை திட்டமிட உதவும் என்றும் இந்த நோயை புரிந்து கொள்வதற்கு இந்த ஆய்வு நமக்கு உதவும் என்று நாங்கள் நம்புகிறோம்.

இந்த ஆய்வில் நீங்கள் கட்டாயம் பங்கு பெற வேண்டுமா?

இந்த ஆய்வில் பங்கு பெற உங்களுக்கு எந்த வித கட்டாயமோ, வற்புறுத்தலோ கிடையாது. உங்கள் முழு விருப்பத்தின் பேரில் மட்டுமே நீங்கள் இந்த ஆய்வில் பங்கு பெற அழைக்கப்படுகிறீர்கள். ஒரு வேளை உங்களுக்கு இந்த ஆய்வில் பங்குபெற விருப்பம் இல்லாவிட்டால், நீங்கள் இந்த ஆய்வில் இருந்து விலகிக் கொள்ளலாம். நீங்கள் அவ்வாறு விலகிக் கொண்டால், அது உங்கள் கண் நோய்க்கு இந்த மருத்துவமனையில் அளிக்கப்படும் சிகிச்சை எந்த விதத்திலும் பாதிக்காது.

உங்கள் தனிப்பட்ட விவரங்கள் நம்பகமான முறையில் பாதுகாக்கப்படுமா?

இந்த ஆய்வின் முடிவுகள் மருத்துவ பத்திரிக்கைகளில் வெளியிடப்படலாம். ஆனால் உங்கள் பெயரோ தனிப்பட்ட விவரமோ எந்த விதத்திலும் வெளியிடப்படமாட்டாது எனினும், இந்த ஆய்வில் நீங்கள் பங்கு பெற்றால் உங்கள் மருத்துவ விவரங்கள் உங்கள் அனுமதியின்றி, ஆய்வு தொடர்பான அதிகரிகளால் மதிப்பாய்வு செய்யப்படும்.

உங்களுக்கு மேலும் ஏதேனும் சந்தேகங்கள் இருந்தால் நீங்கள் **Dr.** ரேஷ்மி மேத்யூ அல்லது **Dr.** ஷீஜா சூசன் ஜான் அல்லது **Dr.** சபன் ஹோரோ ஆகியோரை தெலைபேசி எண்: 0416-2281201 தொடர்பு கொள்ளலாம்.
மின் அஞ்சல்: **reshmimathews19@gmail.com.**

Study title: Role of choroidal thickness and psychological stress in Central serous chorioretinopathy

Consent form

Study Number: _____

Subject's Initials: _____ Subject's Name: _____

Schell hospital no:

CMC hospital no:

Date of Birth / Age (in years): _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]
(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]
(iii) I understand that the researchers conducting this study, others working on the researchers' behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]
(iv) I agree not to restrict the use of any data or results that arise from this study, provided such a use is only for scientific purpose(s). [ ]
(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:

Signature: _____
Or Thumb impression

Date: ____/____/_____

Signatory's Name: _____

Signature of the Investigator: _____
Date: _____/_____/_____
Study Investigator's Name: _____

Signature (or thumb impression) of the Witness:

Signature: _____
Or Thumb impression

Date: _____/_____/_____
Name & Address of the Witness: _____

सेन्ट्रल सीरज कोरियो रेटिनोपथी में कोरोइड् और मनोवैज्ञानिक तनाव का जॉच

अनुमती पत्र

जॉच कमांकः

भाग लेनेवाले का नामः

शेल अस्पताल कमांकः

सी एम सी अस्पताल कमांकः

जन्म तारीख/आयु(वर्षो में):

मै.....पिता/पति का नाम.....

(कृपया रिक्त स्थान में ( ) का चिन्ह अंकित करें।

(1) मै यह घोषित करता/करती हूँ कि मैंने इस जॉच से संबंधित पत्रक में लिखी हुई सभी जानकारी पढ़ी है और इस विषय में मेरी शंकाओं का निरसन हुआ है

( )

(2) मै यह जानता/जानती हूँ कि मेरा इस जॉच में भाग लेना पुर्णतः स्वेच्छा से है और मैं कभी भी अपनी अनुमति वापिस ले सकता /सकती हुँ इससे मेरे उपचारों पर,जो मेरा कानूनी हक है उस पर कोई परिणाम नही होगा।

( )

(3) मै यह जानता/जानती हूँ कि जॉच से संबंधित अभ्यास करने वाले लोग तथा संस्था नियमित समिति के सदस्य मेरी अनुमती बिना,और इस जॉच से मै बाहर होने के बाद भी मेरी स्वास्थ्यविषयक सभी जानकारी देख सकते है। इसके लिए अपनी अनुमति देता/देती हूँ। परंतु मै समक्षता/समक्षती हूँ कि जॉच संबंधित कोई भी जानकारी तथा किसी ब्यक्ति को देते समय,या प्रकाशन या प्रस्तुति करण के समय,मेरी पहचान गुप्त रखी जाएगी।

(4) मै अनुमती देता हूँ/देती हूँ कि मै कभी भी जॉच से उत्पन्न होने वाले परिणामों को नही रोकूँगा/रोकूँगी जब तक ये वैज्ञानिक उद्देश्य के लिए है।

( )

(5) मै यह मानता/मानती हूँ कि मैं स्वेच्छसे इस जॉच में भाग ले रहा रही हुँ

( )

मरीज/कानूनी रूप से स्वीकार्य प्रतिनिधि का हस्ताक्षरः

अंगुठे का निशान

तारीख.....

नामः

जॉचकर्ता का हस्ताक्षरः

तारीख

जॉचकर्ता का नाम

साक्षी का हस्ताक्षरः अंगूठे का निशान

हस्ताक्षरः .....

अंगूठे का निशान

तारीख

साक्षी का नाम

और पैसा

செண்ட்ரல் செரோஸ் கோரியோ ரெட்டினோபதியில் கோராய்டலின் தடிமன் மற்றும் உளவியல் மன அழுத்தத்தின் பங்கு

ஆய்வில் பங்கேற்பதற்கான தகவலறிந்த ஒப்புதல் படிவம்

ஆய்வு எண். ____________

ஆய்வில் பங்குபெறுபவரின் முன்னெழுத்துக்கள் (Initials): ________________

ஆய்வில் பங்குபெறுபவரின் பெயர்: ______________________________

பிறந்த தேதி / வயது: ______________________

1 ____ ____ ______ தேதி அன்று நான் மேற்கூறிய ஆய்விற்கான தகவல் தாளைப் படித்து அதை புரிந்துகொண்டேன் என்று உறுதி அளிக்கிறேன். அது தொடர்பான கேள்விகள் கேட்க எனக்கு முழு வாய்ப்பு இருந்தது.

2 இந்த ஆய்வில் கலந்து கொள்வது ஒரு கட்டாயம் இல்லை என்பதையும், எந்த நிலையிலும் நான் இந்த ஆய்விலிருந்து எந்த காரணமும் அளிக்காமல் விலகிக்கொள்ளலாம் என்பதையும் நான் அறிவேன்

3 இந்த ஆய்வை நடத்தும் அதிகாரிகள் மற்றும் இது தொடர்பான பிற அதிகாரிகள் என்னுடைய மருத்துவ விவரங்களை எனது அனுமதி இல்லாமலே பார்வையிட உரிமை உள்ளவர்கள் என்பதை நான் அறிவேன். ஒரு வேளை நான் இந்த ஆய்வில் இருந்து விலகிக்கொண்டாலும் இது பொருந்தும் என்பதையும் நான் அறிவேன். இதற்கு நான் ஒப்புதல் அளிக்கிறேன். ஆனால் எதன் மூலம் என்னுடைய அடையாளம் வெளியாட்களுக்குத் தெரிவிக்கப்படமாட்டாது என்பதை அறிவேன்.

4 இந்த ஆய்வினால் வெளிவரக்கூடிய தகவல்கள் மற்றும் விளைவுகளை அறிவியல் காரணங்களுக்காகப் பயன்படுத்துவதை நான் தடுக்க மாட்டேன்.

5 மேற்கூறிய ஆய்வில் பங்குகொள்ள நான் ஒப்புதல் அளிக்கிறேன்

ஆய்வில் பங்குபெறுபவரின் கையொப்பம் (அல்லது கைநாட்டை):

நேரி: _____ / _____ / _____

பெயர்: _____

கையொப்பம்:

அல்லது

பிரதிநிதி: _____

நேரி: _____ / _____ / _____

பெயர்: _____

ஆய்வு ஆசாய்ச்சியாளரின் கையொப்பம்: _____

நேரி: _____ / _____ / _____

ஆய்வு ஆசாய்ச்சியாளரின் பெயர்: _____

சாட்சி கையொப்பம்: _____

நேரி: _____ / _____ / _____

சாட்சியின் பெயர் & முகவரி: _____

APPENDIX 3: CLINICAL RESEARCH FORM

Role of choroidal thickness and psychological stress in Central serous chorioretinopathy
Clinical Research Form

Group 1/ Group 2 Date:

Study serial number:

Schell Hospital number: CMC Hospital number:

Name:

Age (years):

Gender: 1. Male 2. Female

State of residence: 1. Tamil Nadu 2. Outside Tamil Nadu (specify state)

Phone:

Educational status:

1. Profession or Honours 2. Graduate or post graduate

3. Intermediate or post high school diploma

4. High school certificate 5. Middle school certificate

6. Primary school certificate 7. Illiterate

Socio economic status: Modified Kuppuswamy's socioeconomic status scale

Education of head of household		Occupation of head of household (last occupation if retired)		Family income per month (per month in Rupees)	
1.Profession or Honours	7	1. Profession	10	1. =30375	12
2.Graduate or post graduate	6	2. Semi-profession	6	2. 15188 – 30374	10
3.Intermediate or post high school diploma	5	3. Clerical, shop owner, farmer	5	3.11362 – 15187	6
4.High school certificate	4	4. Skilled worker	4	4. 7594 – 11361	4
5.Middle school certificate	3	5. Semi-skilled worker	3	5. 4556 – 7593	3
6.Primary school certificate	2	6. Unskilled worker	2	6. 1521 - 4555	2
7.Illiterate	1	7.Unemployed	1	7. =1520	1

Total Score	**Socioeconomic class**
26 - 29	Upper - 1
16 - 25	Upper Middle - 2
11- 15	Lower Middle - 3
5 - 10	Upper Lower - 4
<5	Lower – 5

Clinical Diagnosis (ocular): 1. CSCR 2. No CSCR

Specify ocular diagnosis (in Group 2): Other details (if any):

Affected eye (for Group 1): 1. Right 2. Left 3. Both

HISTORY

Symptoms (for Group 1):1. Decrease in vision 2. Central positive scotoma

3. Metamorphopsia 4. Any other (specify)

Duration of symptoms: 1. < 4 months 2. > 4months

History of:

• Hypertension	0. No	1. Yes
• Diabetes	0. No	1. Yes
• Smoking	0. No	1. Yes
• Alcoholism	0. No	1. Yes
• Dyspepsia	0. No	1. Yes
• Snoring	0. No	1. Yes
• Seasonal cough/wheeze	0. No	1. Yes
• Cardio vascular disease	0. No	1. Yes
• Collagen vascular disorders	0. No	1. Yes

Medications (specify):

Investigations and results:

Refractive error: RE: LE:
(Sphere in dioptres)

Axial length (mm): RE: LE:

Blood pressure (mmHg): Systolic: Diastolic:

SFCT (microns): RE: LE:

Stress score:

Serous RD (microns):

- At the fovea

FA findings (Group 1 – CSCR eye)

- Site 1. Macula 2. Peripapillary 3. Periphery
- Focus 1. Unifocal 2. Multifocal
  No. foci if multifocal-
- Pattern 1. Smokestack 2. Ink blot
- RPE atrophic changes 0. No 1. Yes
  Location 1.macula 2. Peripapillary 3. periphery
- CNVM 0. No 1. Yes

FA findings (Group 1 - fellow eye): 1. Normal 2. Abnormal

If abnormal, 1. RPE atrophic changes
Location 1.macula 2. Peripapillary 3. periphery

2. CNVM 0. No 1. Yes

3. Any other (specify)

Reference for Modified Kuppuswamy's socioeconomic status scale

Kumar N, Kishore J, Gupta N. Kuppuswamy's socioeconomic scale: Updating income ranges for the year 2012. Indian J Public Health. 2012;56(1):103.

APPENDIX 4: COHEN PERCIEVED STRESS SCALE (PSS-10)

COHEN'S PERCEIVED STRESS SCALE

The following questions ask about your feelings and thoughts during THE PAST MONTH. In each question, you will be asked HOW OFTEN you felt or thought a certain way. For each statement, please tell me if you have had these thoughts or feelings: never, almost never, sometimes, fairly often, or very often.

	Never	Almost never	Sometimes	Often	Very often
B1. In the past month, how often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
B2. In the past month, how often have you felt unable to control the important things in your life?	0	1	2	3	4
B3. In the past month, how often have you felt nervous or stressed?	0	1	2	3	4
B4. In the past month, how often have you felt confident about your ability to handle personal problems?	0	1	2	3	4
B5. In the past month, how often have you felt that things were going your way?	0	1	2	3	4
B6. In the past month, how often have you found that you could not cope with all the	0	1	2	3	4

things you had to do?					
B7. In the past month, how often have you been able to control the irritations in your life?	0	1	2	3	4
B8. In the past month, how often have you felt that you were on top of things?	0	1	2	3	4
B9. In the past month, how often have you been angry because of things that happened that were outside of your control?	0	1	2	3	4
B10. In the past month, how often have you felt that difficulties are piling up so high that you could not overcome them?	0	1	2	3	4

Total score -

pss-10s(hindi)

नीचे दिए गए प्रश्न पिछले एक महीने में आपके भावनाओं और विचारो के बारे में पूछा जाएगा कि आपने कितनी बार किसी प्रत्येक रीति में सोचा या महसूस किया है। प्रत्येक प्रश्न के लिए मुझे बताए कि आपके विचार या भावनाएं इनमे से क्या है .कभी नही (0) .लगभग कभी नही (1) .कभी–कभी (2) .अक्सर (3) .अनेक बार (4)					
पिछले एक महीने में,अचानक कुछ अप्रत्याशित बात होने के कारण,आप कितनी बार परेशान हुऍ है।	0	1	2	3	4
पिछले एक महीने में,आपने कितनी बार ऐसा महसूस किया है कि आप अपने जीवन के महत्वपूर्ण (जरूरी) बातो को नियंत्रित नही कर पा रहे है।					
पिछले एक महीने मे आपने कितनीबार ध्वबराहट(बेचैनी) या तनाव महसूस किया है।					
पिछले एक महीने में,अपनी ब्यक्तिगत समस्याओं को सभालने की क्षमता के बारे में आपको कितनी बार आत्मविश्वास महसूस हुआ है।					
पिछले एक महिने में आपको कितनी बार ऐसा लगा है कि सब कुछ थोड़ा बहुत आपकी इच्छा के अनुसार हि चल रहा है।					
पिछले एक महिने में आपको कितनी बार ऐसा लगा है कि आपसे वो सब बाते संभाला नही जा रहा है। जिन्हे आपको संभालना चाहिए।					
पिछले एक महिने में, आप कितनी बार अपने जीवन की परेशानियों को नियंत्रित करने में सक्षम रहे है। नियंत्रित कर पाए है।					
पिछले एक महिने में आपको कितनी बार ऐसा लगा है कि सारी बातें आपके नियंत्रण में है।					
पिछले एक महिने में आपको कितनी बार उन बातों पर गुस्सा आया था,जो आपके नियंत्रण के बाहर थे।					
पिछले एक महिने में आपको कितनी बार ऐसा महसूस हुआ कि कठिनाइयाँ पहाड़ की तरह इतनी ऊँची बन गई है। कि उनपर काबू पाना असंभव नही है।					

PSS – 1 [தமிழ்]

கடந்த ஒரு மாதத்தில் உங்களுடைய எண்ணங்களையும் உணர்வுகளையும் பற்றி கேட்க போறேன். ஒவ்வொரு கேள்விக்கு எத்தனை முறை நீங்கள் இந்த மாதிரி எண்ணங்களுடன் நினைத்தீங்க என்று சொல்லுங்க. ஒவ்வொரு கேள்விக்கும் நீங்க எத்தனை முறை இப்படி நினைத்தீங்க அல்லது உணர்ந்தீங்க என்று சொல்லுங்க.

[எப்பொழுதும் (0) இல்லை, கிட்டதட்ட இல்லை (1), சிலவேளைகளில் (2), அடிக்கடி (3), மிகவும் அடிக்கடி (4)]

		0	1	2	3	4
B1	கடந்த ஒரு மாதத்தில் எத்தனை முறை நீங்கள் எதிர்பாராமல் நடந்த ஒரு விஷயத்திற்கு வருத்தப்பட்டு இருந்தீங்க?					
B2	கடந்த ஒரு மாதத்தில் எத்தனை முறை உங்கள் வாழ்க்கையில் முக்கியமான விஷயங்களை உங்களால் கட்டுப்படுத்த இயலவில்லை என்று உணர்ந்தீங்க.					
B3	கடந்த ஒரு மாதத்தில் எத்தனை முறை மன அழுத்தத்தில் / டென்ஷனில் இருந்தீங்க?					
B4	கடந்த ஒரு மாதத்தில் எத்தனை முறை உங்கள் சொந்த வாழ்க்கையில் உள்ள பிரச்சனைகளை உங்களால் தீர்த்துக் கொள்ள முடியும் என நினைத்தீங்க?					

		0	1	2	3	4
B5.	கடந்த ஒரு மாதத்தில் எத்தனை முறை நீங்கள் நினைத்த விஷயம் உங்கள் வழியில் நடந்தது?					
B6.	கடந்த ஒரு மாதத்தில் எத்தனை முறை நீங்கள் செய்ய நினைத்த எல்லா விஷயங்களையும் உங்களால் செய்ய முடியல என்று நினைத்தீங்க					
B7.	கடந்த ஒரு மாதத்தில் எத்தனை முறை நீங்கள் உங்கள் வாழ்வில் எரிச்சலை கட்டுப்படுத்த முடிந்தது?					
B8.	கடந்த ஒரு மாதத்தில் நீங்கள் எத்தனை முறை எல்லா விஷயங்களையும் கமாளிக்கிறீங்க என்று நினைக்கிறீங்க?					
B9.	கடந்த ஒரு மாதத்தில் எத்தனை முறை உங்கள் கட்டுப்பாட்டுக்கு வெளியே நடந்த விஷயம் - களினால் கோபப்பட்டீங்க					
B10.	கடந்த ஒரு மாதத்தில் உங்களுக்கு வந்த கஷ்டங்கள் ஒன்றன் மேல் ஒன்று வந்து குவிந்த நிலையில் அவற்றை மேற்கொள்ள முடியாது என்று எத்தனை முறை உணர்ந்தீர்கள்?					

APPENDIX 5

(Exclusion criteria – no. 6 - Patients with any other retinal/ choroidal/ optic disc pathology, which may interfere with diagnosis of CSCR, and/ or may be associated with changes in SFCT)

- Diabetic retinopathy
- Hypertensive retinopathy (Grade 3 or 4)
- Retinal vascular occlusions
- Proliferative retinopathies
- Dry or wet age-related macular degeneration
- Choroidal neovascularization
- Any macular pathology other than CSCR
- Optic disc pit/ dysplasia
- Retinal coloboma
- Posterior staphyloma
- Retinal dystrophies/ degenerations
- Choroidal nevus/ hemangioma
- Ocular tumours
- Tapetoretinal dystrophy
- Angioid streaks
- Epiretinal membrane
- Uveitis
- Glaucoma (known case/ use of antiglaucoma medication/ IOP > 21 mmHg on applanation tonometry)
- Amblyopia
- Strabismus

APPENDIX 6

Other medicines that have been implicated in the etiopathogenesis of CSCR

- Antacids
- Anti-reflux medications
- Psychopharmacological medications
- PDE-5 inhibitors
- Antihistaminics
- Sympathomimetics

APPENDIX 7: DATA SHEET

slno	group	date	eyenosh	cmcnosh	name	age	gender	state	place	pnn	edu	se	clin	eye	bv	scotoma	metamor	others
1	1	######	645222s	355108g	shekhar	34	1	2	jharkhar	8.9E+09	2	2	1	1	1	0	0	NA
2	1	######	650103s	'0000000	govindas	47	1	1	NA	8.9E+09	4	3	1	1	1	1	0	NA
3	1	######	642967S	'0000000	shanthi	43	2	1	NA	8.7E+09	7	3	1	1	1	0	0	NA
4	1	######	652765S	'0000000	prabhak	34	1	1	NA	9E+09	5	2	1	1	1	0	0	NA
5	1	######	660576S	'0000000	saravana	45	1	1	NA	9.6E+09	6	3	1	2	1	0	0	NA
6	1	######	636143S	'0000000	velmuru	39	1	1	NA	9.8E+09	4	4	1	1	1	1	0	NA
7	1	######	663739S	'0000000	venkates	35	1	1	NA	7.6E+09	4	2	1	2	1	0	0	NA
8	1	######	670615S	'0000000	balamur	37	1	1	NA	9.7E+08	2	1	1	2	1	0	1	NA
9	1	######	672470s	'0000000	vadivel	35	1	1	NA	9.8E+09	3	3	1	2	1	0	0	NA
10	1	######	687978S	'0000000	Kuppu	35	2	1	NA	9.8E+09	5	4	1	2	1	1	0	NA
11	1	######	590586S	'0000000	rajesh ch	37	1	2	west ber	7.9E+09	2	2	1	2	1	0	0	NA
12	1	######	419875S	'0000000	sunil dir	29	1	1	NA	9.1E+09	2	1	1	1	1	0	0	NA
13	1	######	347169S	'0000000	kumares	36	1	2	karnatak	7.8E+09	2	1	1	2	1	0	0	NA
14	1	######	617280S	'0000000	ajay ram	37	1	1	NA	6.4E+08	2	2	1	1	1	1	0	NA
15	1	######	602710S	'0000000	shankar	49	1	1	NA	9.5E+09	5	4	1	2	0	1	0	NA
16	1	######	703322S	'0000000	biplob ku	43	1	2	bihar	7.8E+09	5	2	1	1	0	1	0	NA
17	1	######	703130S	'0000000	baskarar	44	1	1	NA	8.1E+09	3	3	1	2	0	1	0	NA
18	1	######	471635S	'0000000	debanjar	32	1	1	NA	7.7E+09	1	1	1	2	0	1	0	NA
19	1	######	681736S	531508H	mizanur	46	1	2	banglad	8.2E+09	3	3	1	2	1	0	0	NA
20	1	######	685804S	'0000000	kumarav	38	1	1	NA	1E+10	5	3	1	1	1	0	0	NA
21	1	######	659052s	'0000000	paneer	36	1	1	NA	9.9E+09	4	3	1	1	0	1	0	NA
22	1	######	687218S	'0000000	yuvarani	30	2	1	NA	9.6E+09	3	4	1	1	1	1	0	NA
22	1	######	707758S	'0000000	saravana	39	1	1	NA	8.9E+09	2	2	1	2	0	1	0	NA
24	1	######	708637S	'0000000	senthil k	38	1	1	NA	9.9E+09	2	2	1	2	1	0	0	NA
25	1	######	525877S	'0000000	mala s	52	2	1	NA	9.7E+09	7	4	1	2	1	0	0	NA

slno	duration	days	htn	diabetes	smoking	alcohol	dyspeps	snoring	wheeze	cv ds	collagen	meds	meds sp	csr rel m	csr meds	rel csr ey	rel rel ey	diff rel
1	1	15	0	0	0	0	0	0	0	0	0	1	psychop	1	psychop	0	0	0
2	1	5	1	0	0	0	0	0	0	0	0	0	NA	0	NA	0.75	1	0.25
3	1	14	1	0	0	0	0	0	0	0	0	1	antihype	0	NA	0.5	1	0.5
4	1	30	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.25	0	0.25
5	1	4	0	1	0	0	0	0	0	0	0	1	OHA	0	NA	1	0	1
6	1	14	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1	0.75	0.25
7	1	10	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.75	1	0.25
8	1	60	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.25	0.5	0.25
9	1	14	0	0	0	0	0	0	0	0	0	0	NA	0	NA	-0.5	0	0.5
10	1	14	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.75	0	0.75
11	1	90	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0
12	1	4	0	0	0	0	0	1	1	0	0	0	NA	0	NA	1	0.75	0.25
13	1	30	0	0	0	0	0	1	0	0	0	0	NA	0	NA	0	0.25	0.25
14	1	20	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0.25	0.25
15	1	4	0	0	0	0	0	0	0	0	0	0	NA	0	NA	2	1.75	0.25
16	1	60	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0.25	0.25
17	1	10	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1.25	0	1.25
18	1	110	0	0	0	0	0	0	1	0	0	0	NA	0	NA	0.25	0.25	0
19	1	20	0	1	0	0	0	0	0	0	0	1	OHA	0	NA	-1	-0.75	0.25
20	1	10	0	0	0	1	0	1	0	0	0	1	antihista	1	antihista	-0.25	0.25	0.5
21	1	14	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.5	0.75	0.25
22	1	30	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.5	0.5	0
22	1	10	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1.75	-0.25	2
24	1	30	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1	0.75	0.25
25	1	30	1	0	0	0	0	0	0	0	0	1	antihype	0	NA	0.75	0.75	0

ALcsr ey	ALFel eye	diff AL	bp sys	bp dias	sfct csr	sfctfellow	stress sc	stress cc	srd	fa csr	focus cs	nmbr foc	pallerm c	rpe csr	rparea cs	ped csr	ped area	cnvm csc	fa fel eye	abnfeleye	other	RPEfellc	rpe area	ped fel	pachy cs	pachy fel eye
23.21	23.21	0	120	80	421	368	16	2	296	1	1	1	2	1	1	0	0	0	1	1	4 NA	0	0	0	1	1
22.79	22.69	0.1	160	100	436	393	19	2	585	1	1	1	2	1	1	1	1	0	2	1	NA	1	1	0	1	1
22.69	22.5	0.19	150	80	362	405	19	2	188	1	1	1	2	0	4	1	1	0	1	4	NA	0	0	0	1	1
23.34	23.4	0.06	120	80	382	335	23	2	234	4		0		0	0	0	0	0	2	1	NA	1	1	0	1	1
22.93	22.91	0.02	130	85	356	354	22	2	713	1	2	2	2	1	1	0	0	0	2	1	NA	1	3	0	1	1
22.32	22.32	0	120	60	411	410	22	2	630	2	1	1	2	1	2	0	0	0	2	1	NA	1,1,2		0	1	1
21.65	21.74	0.09	135	77	511	466	23	2	429	1	1	1	1	1	1	0	0	0	2	1	NA	1	1	0	1	1
22.39	22.57	0.18	130	90	249	232	31	3	167	1	1	1	2	1	1	1	1	0	1	4	NA	0	0	0	0	0
22.94	22.96	0.02	110	60	542	511	22	2	186	1	1	1	2	1	1	0	0	0	2	1	NA	1	1	0	1	1
23.21	23.22	0.01	120	90	375	355	28	3	430	1	1	1	2	0	4	1	1	0	1	4	NA	0	0	0	1	1
23.53	23.73	0.2	110	90	417	393	24	2	137	1	1	1	2	0	4	1	1	0	1	4	NA	0	0	0	1	0
23.34	23.63	0.29	130	80	530	469	16	2	239	1	1	1	2	1	1	1	1	0	1	4	NA	0	0	0	1	1
23.04	23.15	0.11	110	70	494	426	17	2	172	1	1	1	1	1	1	1	1	0	2	1	NA	1	1	0	1	1
23.06	23.27	0.21	115	70	454	430	29	3	164	1	1	1	2	1	1	0	0	0	2	1	NA	1	1	0	1	1
23.23	23.12	0.11	120	70	302	391	24	2	589	1	1	1	2	1	1	1	1	0	2	1	NA	1	1	0	1	1
23.72	23.61	0.11	120	80	523	516	27	3	237	1	2	2	1	1	1	0	0	0	2	1	NA	1	2	0	1	1
23.05	23.07	0.02	100	70	402	374	27	3	553	3	1	1	2	1	3	1	1	0	2	1	NA	1	1	1	1	1
22.55	22.83	0.28	110	70	452	448	16	2	214	1	1	1	2	1	1	0	0	0	2	1	NA	0	0	0	1	1
23.68	24.07	0.39	120	80	275	263	23	2	358	1	1	1	1	1	1	0	0	0	2	1	NA	1	1	0	1	1
23.85	23.88	0.17	130	90	406	389	36	3	280																1	1
22.68	22.86	0.18	140	80	478	363	25	2	213	1	1	1	2	1	1	1	1	0	1	4	NA	0	0	0	1	1
22.54	22.61	0.07	110	60	387	333	38	3	113	1	1	1	2	1	1	1	1	0	1	4	NA	0	0	0	1	1
24.05	24.21	0.16	110	80	546	507	23	2	149	3	1	1	2	1	3	1	3	0	2	1	NA	1,1,2,3		1	1	1
23.72	24.03	0.31	110	80	477	390	25	2	188	1	1	1	2	1	1	0	0	0	2	1	NA	1	1	0	1	1
23.01	22.85	0.16	130	80	467	394	20	2	298	1	1	1	2	1	1	1	1	0	2	1	NA	1	1	0	1	1

	grp	date	schel nm	cmc	name	age	gender	state	state of r	mob	edu	SE statu	diag	other
1	2	#####	708919s	0000000	surajit da	47	1	2	west ben	9.6E+08	2	2	presbyop	NA
2	2	#####	6550668S	0000000	shakila b	43	2	2	west ben	7.7E+09	3	4	presbyop	NA
3	2	#####	696733S	0000000	Md sham	42	1	2	west ben	0	5	3	presbyop	NA
4	2	#####	696736S	0000000	sazda kh	41	2	2	west ben	0	6	4	VNL	NA
6	2	#####	700956S	643139F	sunil sing	34	1	2	jharkhan	9.4E+08	2	3	VNL	NA
7	2	#####	363990s	0000000	ashokan	45	1	1	NA	9.8E+09	4	2	ref err	NA
8	2	#####	707848S	0000000	ganesh	37	1	2	west ben	9.2E+09	2	2	VNL	NA
9	2	#####	710624S	0000000	kapil dev	32	1	1	NA	8.1E+09	2	1	VNL	NA
10	2	#####	420594S	0000000	vedamar	50	1	1	NA	9.5E+09	4	4	presbyop	NA
11	2	#####	496881S	0000000	rafeek A	46	1	1	NA	7.9E+09	5	2	presbyop	NA
12	2	#####	707593S	0000000	parames	29	1	2	orissa	8.9E+09	4	3	VNL	NA
13	2	#####	707569S	0000000	anil kum	43	1	1	NA	9E+09	3	2	presbyop	NA
14	2	#####	707548S	0000000	gopikrish	49	1	1	NA	1E+10	4	4	presbyop	NA
15	2	#####	707707S	0000000	samar ku	43	1	2	west ben	9.4E+09	2	2	allergic c	NA
16	2	#####	707711S	0000000	parbati s	31	2	2	west ben	8.8E+09	4	4	Ref err	NA
17	2	#####	698335S	0000000	sanjib sa	45	1	2	west ben	6.3E+07	5	4	presbyop	NA
18	2	#####	700952S	563528H	dolly glor	30	2	2	jharkhan	6.2E+09	2	2	VNL	NA
19	2	#####	708792s	725584h	madhusu	39	1	2	jharkhan	7.8E+09	6	3	ref err	NA
20	2	#####	708568S	0000000	ashly eth	36	2	1	NA	9.8E+09	2	2	VNL	NA
21	2	#####	708839S	0000000	svapon k	31	1	2	banglade	6.3E+08	2	2	VNL	VNL
22	2	#####	708943S	742783H	vishal jyo	38	1	2	Jharkhar	1E+10	2	2	ref err	NA
23	2	#####	708842S	0000000	venjates	38	1	1	NA	9.6E+09	4	2	right low	NA
24	2	#####	708041S	0000000	rajesh pr	47	1	2	bihar	9.6E+07	2	2	presbyop	NA
25	2	#####	708971S	0000000	nilu kum	33	2	2	bihar	8E+09	3	2	VNL	NA
26	2	#####	708970S	0000000	raman ku	43	1	2	bihar	8E+09	2	2	ref err	NA
27	2	#####	708653S	0000000	naresh k	48	1	2	chattisg	7.1E+09	2	2	presbyop	NA
28	2	#####	581416S	0000000	santa ba	39	1	2	west ben	9.2E+09	2	2	ref err	NA
29	2	#####	709063S	746573H	modamn	36	1	2	banglade	9.2E+09	6	2	VNL	NA
30	2	#####	475591S	140347G	liton sah	34	1	2	banglade	0	2	2	ref err	NA
31	2	#####	709160s	0000000	prahlad h	35	1	2	west ben	7.7E+09	3	2	refr err	NA
32	2	#####	707150S	0000000	prakash	37	1	1	NA	0	2	2	ref err	NA
33	2	#####	706394S	527342D	sajal kum	41	1	2	west ben	9.7E+09	2	2	ref err	NA
34	2	#####	709293s	0000000	murali kri	34	1	1	NA	9E+09	2	2	ref err	NA
35	2	#####	538267s	488362g	tapan ch	40	1	2	tripura	9.4E+09	4	2	presbyop	NA
36	2	#####	709751S	0000000	pankaj ku	35	1	2	jharkhan	8E+09	2	2	ref err	NA
37	2	#####	709837S	0000000	kamrude	35	1	1	NA	0	6	4	ref err	NA
38	2	#####	709857S	0000000	sudhaka	38	1	2	bihar	9.8E+09	2	2	presbyop	NA
39	2	#####	595603S	564070g	bogiri ve	37	1	2	andhra	9.9E+09	3	2	VNL	NA
41	2	#####	579221S	0000000	sadiq ba	39	1	1	NA	9.8E+09	5	3	presbyop	NA
42	2	#####	487334S	188530G	ajith kum	39	1	2	west ben	8.6E+09	2	1	ref err,pr	NA
43	2	#####	710943S	0000000	ashish ku	39	1	2	banglade	0	2	1	presbyop	NA
44	2	#####	711057S	0000000	valliamm	53	2	1	NA	9.5E+09	7	5	ref err,pr	NA
45	2	#####	710854S	0000000	md rasel	33	1	2	banglade	0	2	1	VNL	NA
46	2	#####	710519S	0000000	murugan	37	1	1	NA	9.9E+09	6	4	ref err,pr	NA
47	2	#####	710090S	0000000	savarinal	39	1	1	NA	9.6E+09	3	3	presbyop	NA
50	2	#####	345814S	0000000	sampath	40	1	1	NA	9.9E+09	2	1	ref err	NA
48	2	#####	711833s	0000000	mosamn	51	2	2	banglade	0	3	2	presbyop	NA
49	2	#####	449849S	810052F	anees	35	1	1	NA	9.6E+09	2	3	ref err	NA
5	2	#####	711957s	0000000	chandan	37	1	2	west ben	9.7E+09	2	3	VNL	NA
40	2	#####	157216s	0000000	jayson ra	31	1	1	NA	9.9E+09	2	1	ref err	NA

	htn	dm	smoking	alcoholis	dyspepsi	snoring	wheeze	cvds	collagen	meds	med	csr rel m	CSR me	ref RE	reF LE	diff ref	AL RE	AL LE	AL diff	bp sys	bp dias	sfct RE	sfct LE	ped RE	ped LE	pachy RE	pachy LE	stress sc	stress ca	RPE RE	RPE LE
1	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1.75	1.75	0	22.97	22.95	0.02	110	70	240	246	0	0	0	0	6	1	0	0
2	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.75	0.75	0	23.32	23.34	0.02	130	90	227	224	0	0	0	0	20	2	0	0
3	0	0	0	0	0	1	0	1	0	0	NA	0	NA	0.5	0.75	0.25	23.11	23.24	0.13	100	60	294	357	0	0	1	1	11	1	0	0
4	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0	23.45	23.61	0.16	105	75	204	190	0	0	0	0	19	2	0	0
6	0	0	0	0	0	1	0	0	0	1	thyroxine	0	NA	0.25	0	0.25	22.15	22.28	0.13	100	60	284	307	0	0	0	0	10	1	0	0
7	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0.5	0.5	23.07	23.1	0.03	115	75	370	378	0	0	0	0	10	1	0	0
8	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0.5	0.5	23.15	23.22	0.07	100	60	368	376	0	0	0	0	17	2	0	0
9	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1.25	0.75	0.5	23.34	23.33	0.01	80	60	379	396	0	0	0	0	12	1	0	0
10	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1	0.5	0.5	23.34	23.33	0.01	140	80	322	357	0	0	0	0	12	1	0	0
11	0	0	1	0	0	0	0	0	0	0	NA	0	NA	0.75	0.75	0	22.96	22.97	0.01	110	70	390	330	0	0	0	0	10	1	0	0
12	0	0	1	1	0	0	0	0	0	0	NA	0	NA	-1.75	-1.75	0	22.78	22.83	0.05	120	70	369	369	0	0	0	0	8	1	0	0
13	0	1	0	0	0	0	0	0	0	1	OHA	0	NA	-0.25	0	0.25	24.21	24.24	0.03	120	80	261	273	0	0	0	0	8	1	0	0
14	0	1	1	0	0	0	0	0	0	1	OHA	0	NA	0.25	0	0.25	23.26	23.26	0	110	80	315	268	0	0	0	0	6	1	0	0
15	0	0	1	0	0	0	0	0	0	0	NA	0	NA	0.25	0.5	0.25	24.03	24.29	0.26	90	70	317	297	0	0	0	0	9	1	0	0
16	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.25	1	0.25	22.08	22.14	0.06	90	60	300	309	0	0	0	0	7	1	0	0
17	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0.75	0.75	23.23	23.06	0.17	100	60	373	361	0	0	0	0	13	1	0	0
18	0	0	0	0	0	0	0	0	0	1	Flunarazi	0	NA	0	-0.5	0.5	23.39	23.44	0.05	110	60	212	192	0	0	0	0	13	1	0	0
19	0	1	0	0	0	0	0	0	0	1	OHA	0	NA	0.25	0.75	0.5	23.12	23.31	0.19	100	60	347	348	0	0	0	0	11	1	0	0
20	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0	22.95	22.77	0.18	110	60	326	319	0	0	0	0	9	1	0	0
21	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	-0.25	0.25	22.86	23.14	0.28	120	80	374	361	0	0	0	0	10	1	0	0
22	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.75	0.5	0.25	22.32	22.33	0.01	110	70	392	390	0	0	0	0	6	1	0	0
23	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1.5	1.25	0.25	22.79	22.69	0.1	100	70	303	323	0	0	0	0	9	1	0	0
24	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1	0.75	0.25	22.91	22.76	0.15	110	80	305	355	0	0	0	0	11	1	0	0
25	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.5	0.5	0	23	22.93	0.07	120	80	251	248	0	0	0	0	10	1	0	0
26	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0	22.84	22.74	0.1	110	80	301	281	0	0	0	0	12	1	0	0
27	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.5	0.25	0.25	23.76	23.82	0.06	90	60	308	261	0	0	0	0	10	1	0	0
28	0	1	1	0	0	0	0	0	0	1	OHA	0	NA	0.5	0.75	0.25	23.31	23.53	0.22	110	80	275	273	0	0	0	0	6	1	0	0
29	1	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0	22.8	22.86	0.06	110	80	394	367	0	0	0	0	13	1	0	0
30	0	0	0	0	0	0	0	0	0	0	thyroxine	0	NA	0.25	0	0.25	24.34	24	0.34	120	80	341	338	0	0	0	0	8	1	0	0
31	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1.5	0	1.5	22.04	21.86	0.18	100	80	378	385	0	0	0	0	12	1	0	0
32	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0.25	0.25	23.81	23.8	0.01	110	80	337	317	0	0	0	0	11	1	0	0
33	1	0	1	0	0	0	0	0	0	1	antihyper	0	NA	0.5	0.5	0.25	23.57	23.58	0.01	120	70	257	253	0	0	0	0	13	1	0	0
34	0	0	0	0	0	0	0	0	0	0	tegrital	0	NA	-1.5	-1.5	0	23.57	23.58	0.01	110	70	369	349	0	0	0	0	11	1	0	0
35	0	0	1	1	0	0	0	0	0	0	NA	0	NA	0.75	1	0.25	23.97	24.1	0.13	110	70	310	288	0	0	0	0	11	1	0	0
36	0	1	0	0	0	0	0	0	0	0	OHA	0	NA	-1.25	-1.25	0	23.44	23.62	0.18	100	60	339	343	1	0	0	0	12	1	0	0
37	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0	0	0	23.82	23.98	0.16	120	70	364	326	0	0	0	0	13	1	0	0
38	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.25	0.5	0.25	23.8	23.87	0.07	100	70	243	248	0	0	0	0	8	1	0	0
39	0	1	0	0	0	0	0	0	0	1	OHA	0	NA	0.75	0.5	0.25	23.85	23.75	0.1	100	80	251	261	0	0	0	0	11	1	0	0
41	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1.5	1.75	0.25	23.1	23.21	0.11	100	60	295	285	0	0	0	0	13	1	0	0
42	0	0	0	0	1	0	0	0	0	0	NA	0	NA	0.25	0	0.25	23.78	23.83	0.05	100	60	336	358	0	0	0	0	9	1	0	0
43	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.5	0	0.5	23.61	23.8	0.19	110	70	340	375	0	0	0	0	6	1	0	0
44	0	0	0	0	0	0	0	0	0	0	NA	0	NA	2	2	0	22.2	22.05	0.15	100	60	241	277	0	0	0	0	15	2	0	0
45	0	0	0	0	0	0	0	0	0	0	NA	0	NA	1	1.25	0.25	22.83	22.66	0.17	110	70	241	255	0	0	0	0	15	2	0	0
46	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.25	0.5	0.25	23.31	23.29	0.02	100	80	237	275	0	0	0	0	12	1	0	0
47	0	0	1	0	0	0	0	0	0	0	NA	0	NA	0.75	0.75	0	23.26	23.19	0.07	100	70	342	347	0	0	0	0	11	1	0	0
50	0	0	0	0	0	0	0	0	0	0	NA	0	NA	-0.75	-0.75	0	23.39	23.4	0.01	100	70	359	323	0	0	0	0	10	1	0	0
48	0	1	0	0	0	0	0	0	0	1	OHA	0	NA	0	0.5	0.5	22.01	21.94	0.07	80	60	333	275	0	0	0	0	12	1	0	0
49	0	0	0	0	0	0	0	0	0	0	NA	0	NA	0.25	0.5	0.25	22.84	22.77	0.07	110	80	294	249	0	0	0	0	14	2	0	0
5	0	0	0	0	1	0	1	0	0	0	NA	0	NA	0	0.25	0.25	22.62	22.7	0.08	100	70	331	325	0	0	0	0	16	2	0	0
40	0	0	0	0	0	0	0	0	0	0	NA	0	NA	-0.5	-1.25	0.75	23.72	23.65	0.07	100	80	373	384	0	0	0	0	15	2	0	0