

## The Characteristic of Central Serous Chorioretinopathy Patients at Sanglah General Hospital Bali-Indonesia

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**Objective:** to describe characteristics of central serous chorioretinopathy (CSC) patients in Sanglah General Hospital, correlation between visual acuity and foveal thickness before and after oral acetazolamide therapy, the differences of visual acuity and foveal thickness of CSC's patients before and after oral acetazolamide therapy. **Methods:** This study is a descriptive study, than followed by cross sectional study. Data were collected retrospectively from medical report of CSC patients who came to Sanglah General Hospital during period Januari 1<sup>st</sup> 2010 until December 31<sup>st</sup> 2011. **Results:** Central serous chorioretinopathy were found in 22 patients (22 eyes), male predominance (72.7%), majority were in age group 30-40 years (54.55%), and all of cases were unilateral. Most of CSC patients worked as private employees (77.3%). Mean onset patients presented to the hospital was  $14.64 \pm 5.68$  days, with the most common symptom was decreasing vision (86.4%). Mean of follow ups in CSC patients were  $64.11 \pm 6.15$  days. There was correlation between visual acuity and foveal thickness before and after oral acetazolamide therapy, respectively  $r=0.76$ ;  $p=0.001$  and  $r=0.73$ ;  $p=0.001$  (Spearman test). The differences between visual acuity of CSC patients before and after oral acetazolamide therapy was significant ( $0.55 \pm 0.26$  logMAR vs  $0.11 \pm 0.12$  logMAR;  $p=0.001$ ; Wilcoxon test). The differences between foveal thickness of CSC patients before and after oral acetazolamide therapy was also significant ( $484.23 \pm 6.42$  vs  $258.41 \pm 4.21$ ;  $p=0.001$ ; Wilcoxon test). **Conclusions:** CSC patients was male predominance, majority in decade 3-4, all of cases were unilateral and most of the patients worked as private employees. There is a strong correlation between visual acuity and foveal thickness before and after oral acetazolamide therapy. A significant differences found in visual acuity and foveal thickness of CSC's patients before and after oral acetazolamide therapy. In this study, the role of oral acetazolamide in clinical resolution improvement of CSC patients can not be concluded. Further study with control group needed to find it's role.

**Key words:** *Central serous chorioretinopathy, neurosensory retina, visual acuity, foveal thickness*

### INTRODUCTION

Central serous chorioretinopathy (CSC) is an idiopathic condition of the macula which is characterized by serous detachment of the retina neurosensory due to impaired function of retinal pigment epithelium and choroid circulation disorders. In some cases, serous detachment of retinal pigment epithelium was also occurred. CSC is a disease that is self limited and usually affects young men.<sup>1</sup> However role of prophylactic antibiotics is still controversial as no decrease in post operative infection were found since primary and antiseptic procedure can be made to prevent CSC.

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Hernioplasty procedure in Sanglah General Hospital still uses prophylactic antibiotics to prevent CSC, while post-operative infection incidence has yet to be known. The general purpose of this research is to determine the effectiveness of prophylactic antibiotics in patients with hernioplasty in order to evaluate pre-operative procedure in elective hernia that may implicate of reducing cost and bacterial resistance.

CSC classified into acute and chronic. CSC acute if the duration of the illness lasted less than 6 months and found a leak on FFA examination monofocal in the retinal pigment epithelium. Chronic CSC when the duration of illness lasting more than 6 months and found a leak on FFA examination multifocal retinal pigment epithelium.<sup>2</sup> Jackson et al (2008) CSC classified into three acute, chronic and recurrent.<sup>3</sup> Recurrent CSC is that had experienced a clinical resolution, then there was recurrence of disease characterized by

redetachment of retinal pigment epithelium or neurosensory layer.

Various epidemiological studies have consistently demonstrated a high incidence of CSC in men than women.<sup>2</sup> CSC incidence in men is estimated to 9.9% per 100,000 population, while 1.7% in women per 100,000 population.<sup>4</sup> Wang et al (2008) found the incidence of CSC by 79% in males and the remaining women, with an average age of onset was about 45 years.<sup>3</sup> While Siddiqui et al (2008) found the incidence of CSC by 90% in males.<sup>5</sup>

CSC generally occurs in young men aged between 25-55 years. Most cases occur unilaterally. CSC cases are often found in Caucasian, Asian and Hispanic, and rarely in African-American race. Risk factors associated with diseases such as type A personality, CSC, hypochondria, conversion hysteria and neurosis. Other risk factors such as systemic steroid use, pregnancy, alcohol consumption, uncontrolled hypertension is also mentioned play a role in CSC.<sup>1,6,7</sup> CSC certain pathophysiology has not well understood yet. Circulatory abnormalities choroid and retinal pigment epithelium dysfunction suspected as the cause of the CSC. Abnormalities of the choroid circulation ischemia caused local increase in permeability of the choroid. Retinal pigment epithelium to become leaky and tight composition is damaged resulting in abnormal accumulation of choroidal fluid between neurosensory layers and retinal pigment epithelium causing sensory retinal detachments.<sup>8</sup>

Patients with CSC usually present with sudden blurred vision, micropsia, metamorphopsia, central scotoma or parasentral, decreased ability to see color and contrast. CSC patient's visual acuity of 6/6 to 6/60, with a positive lens correction will be lighter or near-normal. External examination of the conjunctiva, cornea, iris and lens appeared normal. Fundus was examined with slitlamp biomicroscopy and indirect ophthalmoscopy, indicates edema of the retina in the macular area with oval shape and clear boundaries (halo).<sup>8</sup> Ancillary test still needed to confirm the diagnosis of CSC. Investigations were conducted using Fluorescein Angiography (FA), optical coherence tomography (OCT), fundus autofluorescence and indocyanine green (ICG) angiography. Examination of the FA is useful to detect leaks on retinal pigment epithelium.<sup>9</sup> Shape characteristic of FA in the case of CSC is the expansile dot pattern, diffuse pattern and smokestack pattern. Examination by OCT is a useful noninvasive method for diagnosis and follow-up resolution on the case of subretinal fluid in CSC patients.<sup>3</sup> In acute CSC, macular region OCT image thickening accompanied by neurosensory or retinal pigment epithelium detachment.<sup>9</sup> Choroid blood vessels abnormalities was detected with ICG angiography.<sup>3</sup>

Initial CSC management is observation for 3-4 months while waiting for spontaneous resolution. This disease usually will heal itself within 8-12 weeks.<sup>3</sup> In a study conducted by Pikkal et al (2002) found oral acetazolamide administration in patients with CSC to accelerate the clinical resolution, but does not affect the final visual acuity and recurrence of CSC.<sup>10</sup> Research conducted by Caccavale et al (2010) showed that low-dose aspirin 100 mg per day has a benefit to accelerate the clinical resolution in patients with CSC.<sup>11</sup> If the patient has not recovered, treatment with laser photocoagulation which aims to close the leak hole in the lining of the retinal pigment epithelium. Photodynamic therapy with verteporvin was used if the leak location close to the center of the fovea.<sup>12</sup> Seong et al (2009) found that the use of anti-VEGF intravitreal injection of bevacizumab in the treatment of acute CSC can speed subretinal fluid resorption.<sup>13</sup>

CSC is generally in good prognosis. As many as 80-90% of cases will experience spontaneous subretinal fluid resorption within 3-4 months, followed by improvement of visual acuity within 6 months to a year after the onset of symptoms.<sup>1</sup> Disease recurrence rate was about 20%. Although normal visual acuity, some patients have permanent visual defects such as decreased sensitivity to color acuity, central scotoma and mikropsia.<sup>2</sup>

This study is made to describe the characteristics of CSC patients who visited the retinal division at Sanglah General Hospital Eye Clinic, to find the correlation between visual acuity and foveal thickness before and after oral acetazolamide therapy, the differences of visual acuity and foveal thickness of CSC patients before and after oral acetazolamide therapy.

## METHOD

This study is a descriptive study, followed by cross-sectional studies (cross-sectional study). Data were collected retrospectively by medical records of CSC patients who come to Sanglah General Hospital. Data taken in this study included age, sex, occupation, onset of arrival, chief complaint, the eye is involved, visual acuity before and after treatment with oral acetazolamide, the thickness of the fovea before and after treatment with oral acetazolamide and average length of follow-up.

The study was conducted at Sanglah General Hospital, Bali-Indonesia in the period of January 1<sup>st</sup> 2010 until December 31<sup>st</sup> 2011. Inclusion criteria were all patients who come for treatment of acute CSC to Sanglah General Hospital during the period of January 1<sup>st</sup> 2010 until December 31<sup>st</sup> 2011 and received oral acetazolamide therapy at a dose of 3 x 250 mg/day with a minimum period of 4 weeks. Exclusion Criteria were patients with incomplete medical records, patients with CSC OCT signal

strength is less than 6, patients with follow-up less than 1 month.

Data were analyzed using SPSS program. Subjects characteristics data were descriptively analyzed and presented as frequency, percentage, mean, and standard deviation. Correlation of visual acuity and foveal thickness before and after treatment were analyzed with *Spearman test*. Analysis of differences in visual acuity before and after therapy as well as differences in the foveal thickness of CSC's patients before and after therapy is performed with *Wilcoxon test*. Value of  $p < 0.05$  was considered significant.

## RESULTS

A number of 32 patients diagnosed during the period of January 1<sup>st</sup> 2010 until December 31<sup>st</sup> 2011 as CSC. Ten patients did not meet the inclusion and exclusion criteria, so the total subjects in this study were 22 eyes of 22 patients. Men have a greater proportion (72.7%) than women (27.3%). Based on age, CSC case most often found in 30-40 years age group by 60%. All cases are unilateral CSC (100%). Most cases of CSC (77.3%) worked in the private sector. The mean onset of CSC's patients presented to the hospital was  $14.64 \pm 5.68$  days, with a chief complaint of the most frequent cause of patients coming for treatment is a decrease in visual acuity (86.4%). The mean length of follow up in patients with CSC was  $64.11 \pm 6.15$  days. CSC type 1 is the largest type (90.1%). The baseline characteristic of study subject were seen in Table 1.

Table 1

Baseline Characteristics of Study Subject	
Patients characteristics	n(%)
Sex : Male	16 (72.7%)
Female	6 (27.3%)
Age: < 30 yo	4 (18.18%)
30-40 yo	15 (54.55%)
≥ 41 yo	6 (27.27%)
Eye involvement	
Unilateral	22 (100%)
Right eye	9 (40.9%)
Left eye	13 (59.1%)
Bilateral	0 (0%)
Occupation	
Private sector	17 (77.3%)
Civil servant	5 (22.7%)
Onset (mean±SD)	14.64±5.68
Chief complaint	
Decrease visual acuity	19 (86.4%)
Floaters	2 (9.1%)
Metamorphopsia	1 (4.5%)
Length of follow up (days)	64.11±6.15
Type of CSC	
Type 1 ( <i>neurosensory detachment</i> )	20 (90.1%)
Type 2 ( <i>RPE detachment</i> )	0
Type <i>intermediate</i>	2(9.9%)

Table 2 shows the relationship between visual acuity and the thickness of the fovea CSC patients before acetazolamide therapy. There was a strong association between visual acuity and the foveal thickness before acetazolamide therapy and was statistically significant ( $r = 0.76, p = 0.001$ ).

Table 2

Correlation Between Visual Acuity and Foveal Thickness Before Acetazolamide Therapy

Parameter	(Mean±SD)	$p^*$
Visual acuity before therapy, logMAR	0.55±0.26	0.001
Foveal thickness before therapy, $\mu\text{m}$	484.23±6.42	

\* *Spearman Test*

Correlation of visual acuity and foveal thickness of CSC patients after acetazolamide therapy can be seen in Table 3. There was a strong association between visual acuity and the foveal thickness after acetazolamide therapy and was statistically significant ( $r = 0.73, p = 0.001$ ).

Table 3

Correlation of Visual Acuity and Foveal Thickness after Acetazolamide Therapy

Parameter	(Mean±SD)	$p^*$
Visual acuity after therapy, logMAR	0.11±0.12	0.001
Foveal thickness after therapy, $\mu\text{m}$	258.41±4.21	

\* *Spearman test*

There was a significant difference of visual acuity of CSC patients before and after acetazolamide therapy ( $0.55 \pm 0.26$  vs.  $0.11 \pm 0.12, p = 0.001$ ), as can be seen in Table 4. There was also a significant difference in the foveal thickness of the CSC patients before and after acetazolamide therapy ( $484.23 \pm 6.42$  vs  $258.41 \pm 4.21, p = 0.001$ ), as seen at Table 4.

Table 4

The Differences of Visual Acuity and Foveal of CSC Patients Before and After Acetazolamide Therapy

Parameter	therapy		$p^*$
	Before	After	
Visual acuity, logMAR (Mean±SD)	0.55 ±0.26	0.11±0.12	0.001
Foveal thickness, $\mu\text{m}$ (Mean±SD)	484.23±6.42	258.41±4.21	0.001

\**Wilcoxon test*

## DISCUSSION

Various epidemiological studies have consistently shown a higher incidence of CSC in men than women.<sup>2</sup> Ciardella, et al (2001) found the incidence of CSC with a ratio of 9: 1 between men

and women.<sup>8</sup> While Zakir et al (2009) in his study found the incidence of CSC in men by 96% with an average age of patients  $37.1 \pm 9.7$  years.<sup>14</sup> Research by Siddiqui et al (2008) found of 30 CSC patients, 90% were male and the remaining women, with a lifespan of 22-55 years, with an average age of 35.4 years.<sup>5</sup> Their study also found patients with CSC occurs more frequently in men (72.7%) than women (27.3%), with a lifespan between 22-47 years, and the highest was found in the age range of 30-40 years (54, 55%). There are no studies that explain exactly why CSC was more frequent in male patients than female. Explanation put forward by Wang et al (2008), among others, because men tend to have a life with higher stress levels, exposure to more crime, average working hours are longer and more financial responsibility is greater.<sup>2</sup> It is said that in the presence of stress conditions, leading to increased levels of cortisol in the circulation. Caccavale et al (2011) and Zakir et al (2009) stated that high cortisol levels in the circulation will result in hypercoagulable and hypoperfusion occur that will ultimately disrupt the choroidal microcirculation.<sup>11,14</sup>

The incidence of CSC on a pilot who works in the United States Air Force is quite high, as many as 47 people of all members having CSC.<sup>2</sup> CSC is often associated with a demanding job deadline, the driver, a job that demands a high sense of urgency and responsibility, as well as a challenging job.<sup>14</sup> In this study, most patients with CSC (77.3%) worked in the private sector. In patient records are not recorded in detail the type of work each of these patients.

CSC can occur unilaterally or bilaterally. Research Siddiqui et al (2008) in the Department of Ophthalmology Medical College and Hospital Chandka Larkana find the majority of cases occur unilaterally CSC that is equal to 86.6%, and only 13.33% bilateral.<sup>5</sup> Gilbert et al (1984) in his study found a case of unilateral CSC as much as 86%, the rest are bilateral.<sup>15</sup> While research Zakir et al (2009) found 23 cases of CSC, all unilateral.<sup>14</sup> Bhende, et al (2006) on OCT examination found neurosensory retinal detachment of the eye of CSC patients who have complaints.<sup>9</sup> Whereas in the asymptomatic fellow eye, it found small picture of epithelial detachment in the temporal fovea. Obtained in this study all patients (100%) with unilateral CSC. OCT examination is only performed on eyes that have complaints. OCT examination of CSC patients should be performed on both eyes, to make sure whether there is any sign of CSC on the eyes without complaint, so it can be ascertained whether the CSC to be unilateral or bilateral.<sup>9</sup>

Research Gilbert et al (1984) found the average onset of the arrival of CSC in patients less than 1 week.<sup>15</sup> While Pikkal et al (2006) in New York found a mean onset of CSC patient's arrival

was 4.05 days (range 1-13 days).<sup>10</sup> In this study, it was obtained, that an average onset of CSC patient arrival to Sanglah Hospital was  $14.64 \pm 5.68$  days. The difference is probably caused by the consciousness of people who diagnosed with CSC who went to the Sanglah Hospital remains low.

CSC Patients usually present with a sudden decrease in visual acuity, central scotoma or metamorphopsia.<sup>2</sup> Spahn et al (2003) found that of 24 CSC patients were studied, as many as 20 people come up with a chief complaint metamorphopsia.<sup>6</sup> Whereas Klein et al (1994) get most of the CSC patients (63%) surveyed came up with the chief complaint of a central scotoma.<sup>16</sup>

In this study, we found that 19 (86.4%) CSC patients came with a chief complaint of sudden decrease in visual acuity, central scotoma rest with complaints and wavy vision (metamorphopsia). This difference may be caused by faulty perception of the patient in the study of the central scotoma or metamorphopsia considered as blurred vision.

CSC is classified into 3 types: type 1 if the detachment occurs in the retina neurosensory layer, type 2 if the detachment occurs in the lining of the retinal pigment epithelium, and type 3 or type in an intermediate layer. Ciardella, et al (2001) found the majority of cases of CSC with Type 1 by 94%, the remainder consisting of CSC type 2 by 3% and 3% are intermediate types.<sup>8</sup> CSC obtained in this study of type 1 in most cases (90.1%) while the rest are intermediate CSC type.

Research carried out by Iida et al (2000) obtain the relationship between visual acuity and foveal thickness in CSC patients.<sup>17</sup> In this research, Iida et al (2000) found the average of foveal thickness in the acute phase of CSC was  $196.9 \pm 22.6$   $\mu\text{m}$  and having an average of foveal thickness of the resolution to be  $124.8 \pm 10.7$   $\mu\text{m}$  ( $p = 0.001$ ). Furuta et al (2009) found the average of foveal thickness in the acute phase of the CSC is 151  $\mu\text{m}$  with an average initial visual acuity was 0.53 (logMAR).<sup>18</sup> After resolution, the average visual acuity to 0.16 (logMAR) with an average of foveal thickness to be 109  $\mu\text{m}$  ( $p = 0.0046$ ).

In this study, we found that there was a strong association between visual acuity and the foveal thickness in CSC patients before and after acetazolamide therapy, and was statistically significant with a value in a row before treatment is  $r = 0.76$ ,  $p = 0.001$  and  $r = 0.73$  after therapy  $p = 0.001$ . Edema caused by fluid accumulation in the area sbretina cause interference with the CSC patient's visual acuity. If the proper fluid accumulation in the central fovea, the complaints that arise will be more clear. With OCT investigation, will appear structurally macular thickness will increase as a result of the edema that occurs.<sup>19</sup>

Research conducted by Pikkal et al (2002) compare among CSC patients treated with

acetazolamide and CSC patients given placebo.<sup>10</sup> The results showed in the group receiving acetazolamide therapy clinical resolution occurs faster compared with the placebo group, but there was no significant difference in final visual acuity of both groups. Chauhari (2004) in his study of CSC patients find oral acetazolamide therapy at a dose of 3x250 mg given for at least 4 weeks to give improved visual acuity in more than 80% of cases, although the results of this study is not a final conclusion because the sample size is still small.<sup>20</sup> Caccavale et al (2010) conducted a study to compare the CSC patients treated with low dose aspirin with CSC patients who received placebo.<sup>11</sup> In the group receiving aspirin therapy clinical resolution occurs more rapidly than the placebo group, but there was no significant difference in final visual acuity of both groups.

In this study, all patients were treated with oral acetazolamide. The average initial visual acuity was  $0.55 \pm 0.26$  and the final visual acuity  $0.11 \pm 0.12$ , with an average length of follow-up of  $64.11 \pm 6.15$  days. Various studies conducted in order to determine the effectiveness of drugs against the CSC patient's final visual acuity. Drugs used such as acetazolamide, propranolol, and aspirin. The study showed an average of more rapid clinical resolution in the treatment group compared to controls, but had no effect on final visual acuity of patients CSC. This is probably due to the role of these drugs is to help improve the circulation of the choroidal blood flow, but could not fix the degeneration of cells already occurred.<sup>2</sup> In this study there was no comparison group, so can not be analyzed how the possible role of acetazolamide in helping to accelerate the clinical resolution in patients with CSC.

## CONCLUSION

In this study, we found a strong association between visual acuity and the thickness of the fovea before and after oral acetazolamide therapy. Also there are significant differences between visual acuity CSC patients before and after oral acetazolamide therapy, as well as significant differences between the thickness of the fovea CSC patients before and after oral acetazolamide therapy. However, in this study the role of oral acetazolamide in clinical resolution improvement of CSC patients could not be concluded. Further study with control group needed to find the role.

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