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# Correlation between color vision with retinal nerve fiber layer thickness in patients diagnosed with papilledema



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## ABSTRACT

**Introduction:** Papilledema results in visual dysfunction, which is often caused by a brain tumor. Decreased color sensitivity may be manifest earlier than visual acuity in papilledema, but the correlation of color sensitivity to retinal nerve fibre layer (RNFL) is not yet determined. Therefore, this study aimed to determine the correlation between color vision and retinal nerve fibre layer thickness in papilledema.

**Methods:** This was an analytic retrospective study with a cross-sectional design using medical records of patients diagnosed with papilledema in the Neuro-Ophthalmology clinic between January 2016 and December 2020.

**Results:** There were 102 patients (204 eyes) enrolled in this study, with a median age was 41 years old. There were 32 (31%) males and 70 (69%) females. Most head CT scan results were intracranial tumors in 88 patients (87.52%). The median value of color vision was 2,63% and the median of retinal nerve fibre layer average thickness was 179,50  $\mu\text{m}$ . Statistical analysis showed a very weak correlation between color vision with retinal nerve fibre layer mean thickness ( $r = 0.185$ ,  $r < 0.2$ ).

**Conclusion:** There is no statistically significant correlation between color vision with RNFL layer thickness in patients with papilledema.

**Keywords:** *papilledema, color vision, retinal nerve fiber layer thickness, optical coherence tomography.*

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## INTRODUCTION

Papilledema—optic disc swelling from elevated intracranial pressure—produces clinically meaningful visual dysfunction across acuity, fields, contrast, and color domains.<sup>1-4</sup> In Indonesia, brain tumors are reported as the most common etiology, with an estimated incidence of 3.4 per 100,000 population.<sup>5-7</sup> Given the risk of irreversible optic neuropathy, timely stratification and objective monitoring are essential.

Pathophysiologically, optic nerve sheath distension compresses peripapillary vessels and disrupts axoplasmic flow, triggering retinal ganglion-cell dysfunction and apoptosis. This process perturbs the parvocellular pathway responsible for high-resolution chromatic processing, manifesting as reduced color sensitivity (dyschromatopsia).<sup>2-4,8</sup> Clinically, color deficits may be subtle or phase-dependent, but they reflect early

neuronal stress within the papillomacular bundle.

Assessment frameworks vary in objectivity. The Frisén scale, though widely used, is observer-dependent and susceptible to intergrader variability. In contrast, optical coherence tomography (OCT) delivers reproducible, quantitative measurements of peripapillary retinal nerve fiber layer (RNFL) thickness and its evolution from edema to potential axonal loss.<sup>9-13</sup> Integrating OCT with functional testing can therefore sharpen disease staging and follow-up decisions.

Importantly, decrements in color sensitivity may precede measurable losses in best-corrected visual acuity in papilledema, positioning color testing as an early functional biomarker.<sup>14,15</sup> However, to our knowledge, no studies have directly quantified the correlation between standardized color vision performance and OCT-derived RNFL thickness in clinically diagnosed papilledema.

Establishing this structure–function linkage could improve risk stratification, optimize surveillance intensity, and inform endpoints for interventional trials. The present study addresses this gap by evaluating the relationship between color vision and RNFL thickness in patients with papilledema.

## METHODS

This was a cross sectional, analytic retrospective study. The sampling was carried out through the medical records of patients diagnosed with papilledema from January 2016 to December 2020. The data was collected after obtaining approval from the Research Ethics Committee Cicendo Eye Hospital, Bandung, Indonesia, with the assigned IRB number: LB.02.01/2.3/055/2021. This study adhered to the Declaration of Helsinki.

The sample size of the study was calculated using the correlation equation:

$$n = \left[ \frac{Z\alpha + Z\beta}{0.5 \ln \left[ \frac{(1+r)}{(1-r)} \right]} \right]^2 + 3$$

n = sample size of the study

Zα = level of confidence 95% (1.96)

Zβ = power of 90% (1.64)

r = correlation coefficient significant 0,494 (based on correlation coefficient from Khalil<sup>13</sup>)

The minimal sample size of the study, base on the equation after adding 10% was 53.

The inclusion criteria were as follows 1) the medical record of papilledema patients verified by a Neuro-Ophthalmology consultant; 2) the head CT scan with contrast results showed the cause of increased intracranial pressure such as intracranial lesions, intracranial hemorrhage, meningitis, etc.; 3) the results of spectral domain Optical Coherence Tomography (SD-OCT) Carl Zeiss Cirrus 5000 HD parameters optic nerve head (ONH) and RNFL by scanning optical disc cube dimensions of 200x200 in patient's both eyes; 4) patients aged > 18 years.

The exclusion criteria were as follows 1) the results of signal strength reliability at low OCT < 5/10; 2) patients who were operated or received treatment from neurosurgery department; 3) history of taking drugs or other substances such as ethambutol, amiodarone, sildenafil, methotrexate and alcohol that cause optic disc swelling; 4) the patient's history of systemic disease includes hypertension, diabetes mellitus, dyslipidemia, stroke, coronary heart disease.

The data collected are age, gender, duration of visual disturbances, color vision assessment using Ishihara plate converted to percentage, average thickness of RNFL, and head CT scan results that showed the cause of increase intracranial pressure.

Statistical analysis used the Kolmogorov-Smirnov test (z) to test the normality of the data and the correlation test with Spearman (ρ). Interpretation of the results based on the strength of the correlation, the direction of the correlation, and the p-value. Calculation of correlation strength (r), based on the criteria of Guilford (1956). The results of

**Table 1. Description of Subject Characteristics**

Variable	N=102 (medical records)
<b>Age (years)</b>	
Median	41
Range (min-max)	19 - 65
<b>Gender</b>	
Male	32(31%)
Female	70(69%)
<b>Duration of visual disturbances (weeks)</b>	
Median	6
Range (min-max)	1 - 52

**Table 2. Description of The Results of Head CT-Scan**

The results of head CT scan	N=102 (medical records)
Intracranial tumors	88 (87,52%)
a. Meningioma	42
b. Astrocytoma	4
c. Glioma	3
d. Pseudotumor	3
e. Craniopharyngioma	3
f. Glioblastoma	2
g. Medulloblastoma	2
h. Schwannoma	1
i. Undescribed	27
Abscess	6 (5,88%)
Intracranial hemorrhage	1 (0,98%)
Subdural hemorrhage	1 (0,98%)
Infarct	2 (1,34%)
Meningoencephalitis	2 (1,34%)
Intracranial metastases	1 (0,98%)
Cerebral venous sinus thrombosis (CVST)	1 (0,98%)

**Table 3. Overview of Color Vision and RNFL Thickness**

Variable	N=204 (eyes)	Normality test (p value)
<b>Color vision (%)</b>		
Median	2,63	
Range (min-max)	0 - 100	
<b>Average RNFL Thickness (μm)</b>		
Median	179,50	0,000
Range (min-max)	72 - 552	

**Table 4. The Correlation Analysis of Color Vision with the Average RNFL Thickness**

Variable	R	p-value
Color Vision with the Average RNFL Thickness	0,185	0,008

the analysis were presented in a table to facilitate data visualization.

## RESULT

The subjects who met the inclusion criteria were 102 patients (204 eyes). The median age was 41 years (range 19-65 years). In this study, 32 patients (31%) were male, and 70 patients (69%) were female. The median duration of visual disturbances

was 6 weeks (range 1-52 weeks). Head CT scan showed intracranial tumors in 88 patients (87.52%), with meningioma in 42 patients (42.72%).

Table 3 shows the results of color vision and the average of RNFL thickness. The median value of colour vision was 2.63% and the median of RNFL average thickness was 179.50 μm (normal value 75 - 107.2 μm).

A data normality test was performed on color vision and RNFL average thickness. The homogeneity of the data was obtained through the Kolmogorov-Smirnov test (z). The results of the normality test for these variables showed that the data distribution was not normal, with p-value of  $<0.05$ .

The correlation test was performed on the color vision variable with the mean RNFL thickness. Statistical analysis was performed with Spearman ( $\rho$ ) due to the non-normal distribution of the data. Statistical analysis showed a very weak positive correlation, so there is no statistically significant correlation between color vision and RNFL layer thickness in papilledema ( $r < 0.2$ ).

## DISCUSSION

Papilledema is mostly caused by intracranial tumors, IIH, obstructive hydrocephalus, meningitis and CVST.<sup>1-3</sup> It can be life-threatening; therefore, the diagnosis of papilledema requires special attention. Kartika et al. stated that a meningioma caused 47.72% of patients with intracranial tumors.<sup>16</sup> This is in accordance with the results in this study that showed intracranial tumors as the main cause of papilledema (87.52%). The most common cause of tumors is meningioma (47.72%).

Raju et al. showed that patients with papilledema caused by intracranial lesions had an average age of 40-50 years, and the majority were female.<sup>17</sup> Crum et al. showed that the incidence of papilledema was in the 4th and 5th decades of life.<sup>18</sup> Neuro-ophthalmic manifestations of intracranial tumor patients conducted by Kartika et al. showed that the majority of patients were female (59.1%) with an average age of 40.14 years.<sup>16</sup> This is the same with this study, which showed the median age was 41 years (range 19-65 years) and the majority of patients (69%) were female.

Color vision test for assessing changes in patient visual function with mild papilledema who have not experienced a decrease in visual acuity. Rehman et al. stated that damage to the parvocellular pathway in papilledema patients affects color vision. Parvocellular pathways are responsible for high spatial resolution, color vision, and subtle stereopsis.<sup>2,3,14,19</sup>

Several studies have been conducted to assess the correlation between color

vision with the condition of the optic disc. Research conducted by Villoslada et al. stated that there is a correlation between color vision and RNFL thickness in multiple sclerosis (MS) patients; however, the same study in patients with papilledema has not been conducted.<sup>14</sup> Wall et al. stated that color vision correlated with visual acuity loss in papilledema patients, but did not correlate with the degree of papilledema based on the Frisén scale. This is because in the study of Wall et al., patients were at a mild degree.<sup>20</sup> In this study, a correlation test was conducted between color vision and the RNFL thickness. The results showed a very weak correlation and were not statistically significant. In this study, the duration of blurring symptoms experienced by patients was at a median of 6 weeks, indicating the possibility of optic disc atrophy disguised by the existing edema condition.

Merticariu et al. stated that there was a correlation between the RNFL thickness and Frisén scale. In the mild-grade group, the average RNFL thickness was 117  $\mu\text{m}$  (95% CI,  $\pm 16\mu\text{m}$ ), the moderate-grade group had an average RNFL thickness of 165  $\mu\text{m}$  (95% CI,  $\pm 89\mu\text{m}$ ), and the high-grade group had 269  $\mu\text{m}$  (95% CI,  $\pm 31\text{ m}$ ).<sup>21</sup> In this study, the average thickness of the RNFL was at a median of 179.50  $\mu\text{m}$ , indicating that the patients were at a moderate level (advanced stage). Color vision is a sensitive test for assessing changes in visual function with mild papilledema. Since our patients were in the moderate-grade group, there was no correlation between color vision and the RNFL thickness in papilledema.

The strength of this study is the larger number of samples than other related studies. The limitation of this study is that there is no assessment of the macular ganglion cell layer (GCL) thickness that could affect the color vision.

## CONCLUSIONS

There is no statistically significant correlation between color vision and RNFL (retinal nerve fiber layer) thickness in patients diagnosed with papilledema. It is necessary to check color vision by using a uniform examination tool for further research and to assess other indicators that can be used as an assessment of visual

prognosis in patients, such as GCL-IPL and its correlation to RNFL and color vision.

## DISCLOSURES

### Funding

None received.

### Ethics Approval

This study had been ethically approved by the ethic committee of Cicendo National Hospital, Bandung, with ethical clearance number: LB.02.01/2.3/055/2021.

### Conflict of Interest

None to state.

### Author Contribution

All authors contributed equally in the writing of this article.

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