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ORIGINAL ARTICLE

THE RELATIONSHIP OF PUPIL SIZE WITH REFRACTIVE EROR IN METABOLIC SYNDROME AND NON-METABOLIC SYNDROME: POPULATION AMONG RURAL POPULATION IN MALANG

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ABSTRACT

Introduction: *This study aims to assess the relationships between pupil size and refractive errors in both metabolic syndrome and non-metabolic syndrome populations residing in rural areas of Malang.*

Methods: *A descriptive study was carried out in 2019 across three villages in Malang districts. All attending participants underwent a comprehensive ocular examination, including pupil size assessment. Pupil abnormalities were defined as deviations from the normal diameter of 2-4 mm in bright light. Clinically relevant refractive errors included hyperopia (SphEq value ≥ 0.25 D), myopia (SphEq value ≤ -0.25 D), and astigmatism (cylinder ≥ 0.25 D). Blood samples gauged serum fasting glucose, high-density lipoprotein cholesterol, and triglyceride levels. Waist circumference, systolic, and diastolic blood pressure were measured. Metabolic Syndrome diagnosis followed the 2006 International Diabetes Foundation criteria. Participants were categorized into metabolic syndrome and non-metabolic syndrome groups.*

Discussion: *The examination involved 953 participants, encompassing 944 right eyes and 942 left eyes. For the right eye, 434 eyes showed emmetropia, 252 exhibited myopia, 141 had hyperopia, and 117 presented astigmatism. Pupillary abnormalities were linked to astigmatism, but lacked significance (p = 0.893). The left eye results indicated 444 eyes with emmetropia, 244 with myopia, 138 with hyperopia, and 116 with astigmatism. Correlation with pupillary abnormalities yielded a non-significant p-value of 0.864. Pupil size outcomes in metabolic syndrome (499 eyes) and non-metabolic syndrome (454 eyes) were not significant (p = 0.649).*

Conclusion: *Refractive error does not correlate with pupil size in metabolic syndrome and nonmetabolic syndrome.*

Keywords: *Pupil, Pupil size, Pupillary abnormality, Refractive Error, Myopia, Hyperopia, Astigmatism, metabolic syndrome*

INTRODUCTION

Refractive error is a global vision problem and is the second leading cause of preventable blindness. According to the 2013 Riskesdas, the prevalence of refractive disorders was 9.5%, while the corrected prevalence was only 4.6%.[1]

The pupil is an important factor in evaluating the visual system. When there is a change in the size of the pupil diameter, the goal is not only to control the amount of light, but most

importantly as an optical system. The diameter and location of the pupil are very important in refractive surgery.[2-3]

Normal pupil size depends on the intensity of retinal illumination, the proximity of stimuli, and the emotional state of a person.[2-3] There are theories suggesting a relationship between pupil size and refractive errors, although the results are controversial. The pupil forms the physical opening barrier of the eye's optical system which controls retinal illumination and retinal image quality.[2-4] Many studies conducted that there is a tendency for myopic subjects to have larger pupils than hyperopic and emmetropic subjects.[2,3,4]

Metabolic syndrome (SM) is a collection of interconnected diseases characterized by central obesity, hypertension, dyslipidemia and hyperglycemia. The cause of SM is not known with certainty but is closely related to insulin resistance, visceral adiposity, atherogenic dyslipidemia, and endothelial dysfunction.[4,5,6] The prevalence of SM according to Riskesdas (2007) was 17.5% while in the 2013 Riskesdas the prevalence of SM in Indonesia was 23%.[17] The criteria for SM based on IDF include central obesity plus 2 of the following 4 factors, namely hypertriglyceridemia, low high density lipoprotein cholesterol (HDL-C), hypertension, and hyperglycemia.[7]

Metabolic syndrome triggers extensive tissue damage including the eye due to increased oxidative stress, inflammation and endothelial dysfunction[4,5] The components of the metabolic syndrome such as diabetes, hypertension, and obesity will cause autonomic function disturbances which cause disturbances of sympathetic and parasympathetic activity.[4,5]

This population-based study was conducted in Malang Regency and aimed to determine the relationship between pupil size and refractive errors in populations with metabolic syndrome and non-metabolic syndrome in Malang Regency

RESEARCH METHODS

This research has received approval for ethical clearance from the ethical commission for health research, Faculty of Medicine, University of Brawijaya with letter number No.211/EC/KEPK/07/2019. This research is descriptive-research on population (population based) with a cross sectional study design with consecutive sampling conducted in Mendalanwangi, Sidorahayu and Cepokomulyo villages, Malang Regency. Data collection was carried out on July 2019 - November 2019, then data processing was carried out in January 2020 - July 2022.

The research group consisted of people who came for the initial check-up in 3 villages during that period. The inclusion criteria in this study were respondents who were included in

Ophthalmol Ina 2023;Supplement Ed.:1-9

the SMARTHEALTH population and had refractive errors. The research subjects carried out a complete initial examination including examination of blood pressure, abdominal circumference, height, and weight. The patient also had an visual acuity examination: *Visus naturalis*, BCVA, pupil diameter. Blood tests after fasting for at least 8 hours such as checking fasting blood sugar (GDP), Triglycerides (TG), and High-Density Lipoprotein (HDL) were also completed in research subjects.

Metabolism in this study was taken from International Diabetes Federation (IDF) criteria. Central obesity with criteria on male ; abdominal circumference > 90 cm and female > 80 cm or Body Mass Index > 30, and there are 2 of 4 other criteria as follows: Triglycerides > 150 mg/dL or have taken triglyceride drugs, HDL < 40 mg/dL in men and women < 50 mg/dL or have taken anti-cholesterol drugs before, systolic blood pressure ≥ 130 mmHg or diastolic ≥ 85mmHg or have taken anti-hypertensive drugs, and Fasting blood sugar ≥ 100 mg/dL or previously diagnosed with DM.[18] All data was processed using STATA 14. To find out the relationship between variables using a logistic regression test.

DISCUSSION

In this study dominated by female respondent (76.6%) with an age range of 50-59 as many as 387 (40.6%) as shown in table 1.

Table 1. Demographic Characteristics

Variable	N	(%)
Gender		
Male	223	23.40
Female	730	76.60
Age (Years)		
40-49	262	27.42
50-59	387	40.65
>60	304	31.93

Table 2. Clinical Characteristics

Variable	N	(%)
DM		
No	765	84.16
Yes	144	15.84
Hypertension		
No	380	39.87
Yes	573	60.13
BMI		
Normal	657	68.94
Obesity	296	31.06
TG		
Normal	627	68.90

High	283	31.10
HDL		
Normal	546	57.29
Low	407	42.71
Central Obesity		
No	231	24.24
Ya	722	75.76
Pupil Diameter		
Normal	669	71.17
Abnormal	271	28.83
Dyslipidemia		
No	395	43.41
Ya	515	56.59
Metabolic Syndrome		
No	499	52.36
Yes	454	47.64
Refractional Status OD		
Emetropia	434	45.97
Miopia	252	26.69
Hipermetropia	141	14.94
Astigmatisme	117	12.39
Refractional Status OS		
Emetropia	444	47.13
Miopia	244	25.90
Hipermetropia	138	14.65
Astigmatisme	116	12.31

Of the 953 respondents, 944 were examined for the right eye and 942 for the left eye with an age distribution where emmetropia was obtained to be similar in both eyes. Refractive errors were found similar in both eyes where myopia was the most refractive error in the right eye (26.69%) and left eye (25.90%) followed by hyperopia and astigmatism. Characteristics for the components of the metabolic syndrome such as DM were 765 correspondents, hypertension 573, obesity 297, low HDL 407, central obesity 722, dyslipidemia 515 respondents.

This study is dominated for normal pupil diameter for SM respondents there were 47.64% 52.36%. The SM and non-SM populations were almost the same (table 2)

Table 3. Correlation between Pupil Size and Variables

Variable	Nomal	Abnormal	*p-value*
Age (Years)			
40-49	218	43	**0.000***
50-59	271	108	
> 60	180	119	
Gender			
Female	135	83	**0.001***
Male	534	188	
DM			
No	538	217	0.879
Yes	101	42	

Hypertension			
No	276	103	0.357
Yes	393	168	
BMI			
Normal	453	194	0.243
Obesity	216	77	
TG			
Normal	444	175	0.597
High	196	84	
HDL			
Normal	378	157	0.688
Low	291	114	
Central Obesity			
No	147	78	**0.029***
Yes	522	193	
Dyslipidemia			
No	274	113	0.823
Yes	366	146	
MetS			
No	347	145	0.649
Yes	322	126	
Refractional Status OD			
Emetropia	299	125	0.893
Miopia	177	73	
Hipermetropia	100	41	
Astigmatisme	86	30	
Refractional Status OS			
Emetropia	308	129	0.864
Miopia	172	70	
Hipermetropia	96	41	
Astigmatisme	84	29	

Based on table 3 and table 4 it can be seen that pupil size is significantly related to the age and gender (p-value <0.005). For SM components such as DM, HT, HDL, dyslipidemia is not significantly related to pupil size. In the SM and SM populations, there was no significant relationship to pupil size.

Table 4. Factors associated with Pupil Abnormality

Variable	**Multivariate Regression Analysis**		**Multivariate Regression Analysis**	
	OR (95% CI)	**p-value**	**OR (95% CI)**	**p-value**
Age (Years)				
40-49	Ref		Ref	
50-59	1.98 (1.32-3.01)	0.001*	1.94 (1.30-2.89)	0.001
> 60	3.07 (1.99-4.73)	0.000*	3.12 (2.07-4.69)	0.000
Gender				
Female	Ref		Ref	
Male	1.35 (0.92-2.00)	0.125	1.49 (1.05-2.11)	0.024
DM				
No	Ref			
Yes	0.97 (0.64-1.47)	0.881		
Hypertension				

No	Ref			
Yes	1.03 (0.75-1.43)	0.839		
BMI				
Normal	Ref			
Obesity	1.08 (0.75-1.55)	0.689		
TG				
Normal	Ref			
High	1.1 (0.78-1.55)	0.590		
HDL				
Normal	Ref			
Low	1.07 (0.78-1.46)	0.687		
Central Obesity				
No	Ref			
Yes	0.85 (0.56-1.29)	0.438		
SM				
No			Ref	
Yes			1.13 (0.84-154)	0.431
Refractional Status OD				
Emetropia	Ref		Ref	
Miopia	0.93 (0.59-1.45)	0.743	0.92 (0.60-1.43)	0.715
Hipermetropia	0.83 (0.45-1.53)	0.552	0.88 (0.49-1.58)	0.670
Astigmatisme	0.86 (0.47-1.56)	0.608	0.91 (0.50-1.64)	0.748
Refractional Status OS				
Emetropia	Ref		Ref	
Miopia	1.09 (0.69-1.72)	0.705	1.09 (0.70-1.70)	0.692
Hipermetropia	1.14 (0.62-2.08)	0.680	1.15 (0.64-2.08)	0.628
Astigmatisme	0.85 (0.47-1.55)	0.602	0.89 (0.49-1.61)	0.704

Table 4 also shows that there is a significant relationship between the ages of 50-59 years with a p value of 0.001, which means that there is an increase in the occurrence of pupillary defects 1 times greater than the 40year-old group. In respondents aged more than 60 years there was a 3 times greater increase in probability in the occurrence of pupillary abnormalities (p value 0.000). It was concluded that older age is more at risk of having pupil size abnormalities. In refractive errors, myopia, hypermetropia and astigmatism are not significantly associated with pupil size p value> 0.005. In the population with metabolic syndrome and non-metabolic syndrome, it is not significantly related to pupil size as well as to the SM component. Gender did not have a significant difference between men and women.[3]

Based on some literature, age is one of the most important factors that influence pupil activity and shape. Scotopic, mesopic, and photopic pupil diameters decrease with age because accommodative ability decreases with age. With age, the shape of the pupil changes from a regular circular shape to an irregular shape. Pupil response slows down with age. Hippus pupils at high frequency also decrease with age. This suggests that the maximum speed of pupillary contraction and dilation also decreases with age. [8,9]

Several previous studies have shown that older people have smaller pupil diameters at rest in the dark than younger people. The reduced amplitude of the dark reflex and the prolonged recovery time of the light reflex are consistent with the decreased sympathetic activity that occurs with old age. There is independent evidence that the sympathetic and parasympathetic components of the autonomic nervous system change differently with age.[8-10]

Changes in pupil size by age indicate that the pupillary system is very sensitive, reflecting the normal aging process. It has been suggested that the decrease in resting pupil size with increasing age is caused by degeneration of the senile iris leading to increased rigidity.[5] Such a mechanism might explain the reduced light reflex amplitude or rate of constriction, either directly or through a reduction in pupil size at rest.[11-13]

Older individuals have smaller pupil diameters, consistent with sympathetic deficit or parasympathetic disinhibition. There was reduced dark reflex amplitude and rate of dilation, consistent with sympathetic deficit. Furthermore, older subjects had a prolonged pupillary light reflex recovery time, consistent with sympathetic deficits. Pupil shape also shows age-related changes, possibly due to structural changes such as changes in muscle fiber contractility, stromal atrophy with loss of connective tissue, and hyaline degeneration.[5,14]

The results of this study also found no significant difference between the type of refractive error and pupil size. The relationship between the type of refractive error and pupil size is still a matter of controversy where the results of existing studies are conflicting. As the magnitude of the refractive error increases, the size of the pupil decreases. This relationship may be the result of other factors such as axial length and anterior chamber depth. All of these factors are known to be greater in myopia.[16]

The results of this study are in accordance with other studies where the result is that accommodation is not enough to push the pupils closer to responding. This study expands on previous research which also included myopia and hyperopia subjects.[17,18] This shows that the pupils are controlled by the pupillary light reflex.[2]

Osaiyuwu and Atuanya found that there were significant differences in pupil size in myopia, hypermetropia and emmetropia.[3] Myopia has larger pupils compared with emmetrope and hyperopia, when the refractive error is not corrected. However, the accommodation response was not measured or controlled, target luminance was not standardized, and pupil diameter was measured subjectively.[2]

In this study, pupil size did not have a significant relationship in the population with metabolic syndrome and non-metabolic syndrome. In patients with DM, autonomic neuropathy occurs which causes abnormalities in the diameter of the pupil size, such as the study of

Karavanaki et al., but in this study there was no significant relationship between pupil size and DM, possibly due to the duration of the development of autonomic neuropathy abnormalities in the DM correspondent.[18] Hypertension causes impaired autonomic function which increases the sympathetic autonomic activitiy. In this study, no significant relationship was found between hypertension and pupil size.[19] In Petra et al's study there was also an autonomic nervous system disorder which caused a decrease in sympathetic and parasympathetic activity, while in this study there was no significant relationship.[20]

The weakness of this research is the lighting that is not the same at the place where the research is carried out. Measuring pupil size and determining the correct pupil diameter under different lighting conditions is a complex and difficult task. The main reason for this complexity is that the pupil is not static and the size of the pupil always differs even under the same light level.[16]

This different lighting issue can also lead to biased results from this study so that the advice we give is to carry out further research with pupil measurements carried out in a dim room or in a room that has the same lighting. A good pupil measurement is in a dim room.[18]

CONCLUSION

From the results of this study, there was no significant relationship between pupil size and refractive error in metabolic syndrome and non-metabolic syndrome and there was also no significant relationship between pupil size, sex and components of the metabolic syndrome. Age is a factor that causes an increased risk of pupillary size abnormalities.

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