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RELATIONSHIP BETWEEN PLATELET COUNT, PDW, PCT, AND MPV WITH VISUAL FIELD DEFECT IN PRIMARY OPEN ANGLE GLAUCOMA

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Abstract. Glaucoma is a multifactorial disease and the second leading cause of irreversible blindness worldwide, and incidence of open-angle glaucoma more frequent, including in Indonesia. The etiology is still unclear, but the risk factors are the immune system and increased systemic microvascular abnormalities affected by platelets. **Objective.** The purpose of this study was to determine the relationship between platelet parameters and visual field defect in POAG. **Methods.** This research is an analytic study with a case control design. Respondents are 30 POAG patients and 30 normal subjects as a control in Universitas Sumatera Utara Hospital and Satellite Hospital from August to December 2021. Venous blood samples were taken as much as 3 cc to assess platelet parameters, then analyzed in the clinical laboratory. Each group was examined with Humphrey's Perimetry which was further classified based on Hodapp Anderson Parrish criteria. **Results.** Most subjects in the POAG group are male, 53.3%. In POAG group the mean values of platelet count 267.28 103/µL, PDW 11.41 fL, PCT 0.25%, and MPV 9.49 fL. **Conclusion.** There was an increase in PDW values in advanced POAG patients, but no significant differences were found in visual field defect between the two groups.

Keyword: Platelet, POAG, Visual Field

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1 Introduction

Glaucoma is a diverse and multifactorial neurodegenerative disease characterized by optic neuropathy with cupping and visual field defects, with POAG highest prevalence.[1] Data from the Indonesian Ministry of Health (2015) stated the overall prevalence of glaucoma was about 2.53%, while the prevalence of POAG in Sanglah General Hospital was approximately 44.6% at the age of 50-59 years.[2][3] Numerous risk factors such as increased intraocular pressure, vascular, genetic, metabolic, toxic, free radical, and dysregulated immune system of toll-like receptor 4 (TLR4) receptors associated with changes in trabecular meshwork fibrosis and neuroinflammation in optic nerve also play an essential role.[4][5]

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Platelet activation with the vascular endothelium and plasma components plays an essential role in the pathophysiology of thrombosis and microvascular processes that affect ocular microcirculation. Dysfunction of platelets in POAG contributes to developing comorbidity of microvascular disease and damage to Retinal Ganglion cells (RGC) in glaucoma. Some studies mentioned that the assessment of platelet function and activation could evaluate glaucoma condition. Increasing procoagulant and fibrinolysis can cause a hypercoagulative state in POAG. Its component can involve prothrombin, thrombin, fibrinogen, plasminogen activator inhibitors, and fibrin D-dimer that will affect the perfusion of retinal blood flow and optic nerve so that the occurrence of the visual defect.[4][6]

2 Methods

An analytical case-control study consists of 30 POAG patients and 30 normal control subjects. The enrollment was performed consecutively at Eye Polyclinic, Glaucoma Division in Universitas Sumatera Utara Hospital, and Satellite Hospital from August to December 2021. This research was established by the standards of ethics Declaration of Helsinki and approved by the Faculty of Medicine Universitas Sumatera Utara ethical committee. Informed consent was collected from all subjects and written in the form.

All subjects had gone through screening inclusion and exclusion criteria. Exclusion criteria are patients with anterior segment abnormalities, intraocular postoperative or ocular trauma, posterior segment abnormalities, medical problems related to thrombosis, Thalassemia, history of repeated transfusions, history of malignancy, hemodialysis, chemotherapy, thyroid disease, hyper aggregation or hypoaggregation and autoimmune disease, use of antiplatelet or anticoagulant drugs within 1 week. All subjects underwent ophthalmologic examination, including visual acuity, anterior segment examination under slit-lamp (Righton), gonioscopic testing (Ocular Three Mirror Universal Laser Lens) to evaluate the angle structure, and direct ophthalmoscopy to evaluate posterior segments. A venous blood sample of 3 cc was performed at the Clinical Pathology Laboratory University of Sumatera Utara. Platelet count, PDW, PCT, and MPV were then analyzed with an automated hematology analyzer (Sysmex XN 1000, Japan).

This study was analyzed using the T-independent test, Mann Whitney and Kruskal Wallis, Pearson correlation test if the data were normally distributed, and the Spearman correlation test if otherwise. All data were processed by using SPSS software version 22.0. The p value, which shows results less than 0,05, means that the research is statistically significant.

3 Results

The study subjects were predominantly male in the study group (53.3%) and females in the control group (56.7%). The mean age in the POAG subjects was 55.73 years and 43.27 years in the control group. Clinical and demographic parameters showed no significant differences in gender, age,

and visual acuity. Still, there were significant differences in IOP, VCDR, RNFL, MD perimetry, and RNFL Thickness between POAG and controls (p<0.05). Other characteristics can be seen in Table 1.

Table 1. Characteristics Distribution of the Participants

Characteristic	POAG	Control	p value
Gender, n (%)			
Man	16 (53,3)	13 (43,3)	<0,505[a]
Woman	14 (46,7)	17 (56,7)	
Age, year			<0,199[b]
Average (SD)	55,73 (13,09)	43,27 (7,74)	
BCVA, logMAR			<0,001[a]
Average (SD)	1,21 (1,12)	0,11 (0,16)	
IOP, mmHg			<0,001[b]
Average (SD)	26,17 (6,95)	15,23 (2,11)	
VCDR			<0,001[b]
Average (SD)	0,78 (0,13)	0,32 (0,1)	
MD Value			<0,001[b]
Average (SD)	-12,99 (8,28)	-3,63 (2,2)	
Visual Field Defect			
Early	8 (26,7)	28 (93,3)	<0,001[a]
Moderate	6 (20)	2 (6,7)	<0,001[a]
Advanced	16 (53,3)	0	
RNFL Thickness			<0,001[b]
Average (SD)	81,47 (22,33)	103, 47 (14,33)	

[a]*Chi Square,* [b]*T Independent, cMann Whitney*

The difference in Platelet Count, PDW, PCT and MPV between POAG and Control Groups

Table 2, the difference in platelet count, PDW, PCT and MPV values in POAG and control groups. Platelet count, PDW, and PCT level showed statistical significance (p< 0,05 between the two groups.

Table 2. The difference in Platelet Count, PDW, PCT and MPV between POAG and Control Groups

Platelet Index	POAG	Control	p value
Platelets, 103/µL			
Average (SD)	267,28 (56,92)	314,1 (57,15)	0,002[a]
PDW, fL			
Average (SD)	11,41 (1,7)	10,49 (1,15)	0,029[a]
PCT, %			

Average (SD)	0,25 (0,06)	0,3 (0,05)	0,002[b]
MPV, fL			
Average (SD)	9,49 (0,91)	9,68 (0,63)	0,339[b]

[a]*Mann Whitney,* [b]*T Independen*

Table 3. The Relationship of Platelet Parameters with Visual Field Defect

		Visual Field Defect			p
		Early	**Moderate**	**Advanced**	
POAG	Platelet Count	263,38 (74,98)	269,57 (67,5)	268,38 (45,92)	0,704[a]
	PDW	11,16 (1,62)	11,46 (1,66)	**11,52 (1,84)**	0,939[a]
	PCT	0,24 (0,07)	**0,27 (0,07)**	0,25 (0,05)	0,672[b]
	MPV	9,14 (0,98)	**10,06 (0,44)**	9,45 (0,94)	0,144[a]
Control	Platelet Count	310,21 (570,79)	368,5 (205,06)	-	0,096[c]
	PDW	10,51 (1,17)	10,15 (1,06)	-	0,617[c]
	PCT	0,29 (0,05)	0,35 (0,01)	-	0,065[c]
	MPV	9,7 (0,65)	9,45 (0,35)	-	0,428[c]

[a]Kruskal Wallis, [b]Anova, [c]Mann Whitney

From this study, the highest PDW mean showed in advanced, and also mean PCT and MPV in moderate. However, there is no significant association between platelet count, PDW, PCT, and MPV with visual field defect.

4 Discussion

POAG is the majority glaucoma type worldwide. The multifactorial conditions contribute to the vascular abnormality, leading to ischemia in the optic nerve head, causing glaucomatous injury. Furthermore, it can increase the production of procoagulant platelets, thrombin generation, rheological changes in blood cells, and changes in the central nervous system. TLR4 mediates this change is prothrombotic. Recent evidence showed that TLR4 and the complement system are related to innate immunity and hemostasis and contribute to systemic microvascular damage and neurodegeneration in POAG.[5]

Based on table 1, male is predominant in the study group; Deva, Suryathi, Kusumadjaja in Bali (2020) and Ma et al in Shanghai (2019) also conducted the similarity.[3,6] Based on the theory, there are differences in the anatomical structure of the eyes between males and females, where males have a longer axial length of the eyeball, shallower anterior chamber, more prominent area of the disc, thinner RNFL and higher IOP. The ocular hemodynamic influences, such as the effect of estrogen vasodilators, affect eye blood flow. Thus, during menopause, women have the same risk as men for POAG occurrence due to decreased estrogen-meditated protection.[7][8][9][10]

The mean age of POAG subjects is 55.73 years, consistent with the Singh et al. study in Nepal (2020), where the mean age of POAG subjects was 54.75±15.62 years. Pavlijasevic S et al (2009)

explained that older age and metabolic abnormalities are genetically predisposed factors to appear glaucoma, especially POAG.[11][12]

This study has significant differences in IOP, VCDR, RNFL thickness, and MD perimetry between POAG and controls ($p<0.05$). The IOP is one of the most critical risk factors for glaucoma. High IOP causes damage to the optic nerve either by direct mechanical damage to the retinal nerve fiber layer or ischemic injury from compression of the blood vessels supplying the optic nerve head and also describes a cell loss and retinal ganglion axon that reflects a thinning of the neuroretinal rim thus triggering glaucomatous damage.[13]

The PDW parameter reflects the heterogeneity of platelet volume and platelet activation markers. Metabolically large platelet sizes become more active and potentially significant as prothrombotic, producing more Ib glycoprotein receptors and IIb/IIIa glycoprotein receptors, releasing more A2 thromboxane, and having faster aggregation capabilities.[16] So it also correlates this condition with the advanced of POAG in this study. However, no significant relationship was found. The MPV parameter reflects large platelet volumes allow the aggregation ability to be more substantial than platelets with small volumes. This is due to an increase in the production of A2 thromboxane and an increase in the expression of glycoprotein IB and glycoprotein IIB/IIIA receptors on its surface. This supports the hypothesis that hypercoagulation processes occur in POAG patients. [14][15]

Although there was no significant relationship between platelet parameters and the visual field defect in this study, but there is a potential relationship between platelet parameters and the incidence of POAG. The limitations of this study are single-center, so it is recommended that large-scale research is needed, and multi-center prospective studies are expected to provide a better understanding of finding the relationship between platelet parameters and POAG. Further research is needed on other variables, especially those related to haematovascular components that affect the visual field defect in POAG.

5 Conclusion

There was an increase in PDW levels among POAG patients in the advanced category. Still, no significant differences were found between the study and control groups on the degree of visual field defect.

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