ABSTRACT

**Background:** Diabetic retinopathy (DR) is the most common microvascular complication of diabetes. Several studies have emphasized the importance of platelet activation in the pathogenesis of DR. Platelet activation can be known by examination of platelet indices, namely Mean Platelet Volume (MPV), and Platelet Distribution Width (PDW).

**Objective:** This study aims to determine the relationship between MPV, PDW and staging of DR, as one of the markers of disease progression.

**Methods:** This study is a cross-sectional study at Sanglah Eye Clinic conducted from July to October 201. A total of 51 samples with DR were categorized based on the staging of DR, namely Non-Proliferative DR (NPDR) and Proliferative DR (PDR). Each group of staging was performed platelet indice (MPV and PDW).

**Result:** The correlation coefficient (r) was obtained -0.75 (p = 0.603) for MPV. Logistic regression test between MPV value and DR showed no association between MPV increasing and DR staging. B value 0.015, with Odd Ratio (OR) 1.015, 95% confidence interval and p value = 0.944. Spearman correlation test between PDW and DR staging obtained correlation coefficient (r) of = 0.006 (p=0.967). Logistic regression test between PDW value and diabetic staging of retinopathy showed no correlation between increasing PDW and degree of DR. B value 0.148, with Odd Ratio (OR) 1.160, 95% confidence interval and p value = 0.592.

**Conclusion:** This study showed that there is no correlation between Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and the degree of DR.

**Keyword:** Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), degree of Diabetic Retinopathy (DR).


INTRODUCTION

Diabetes Mellitus (DM) is one of the chronic diseases, which is decrease the insulin secretion and increasing insulin resistance in the body. Diabetes mellitus is a leading cause of metabolic disorder worldwide. Data from World Health Organization (WHO) showed about 346 million people worldwide suffer from diabetes in 2011. In Indonesia there were 8 million people suffering from DM in 2000 and estimated increasing in number of 21 million people in 2030. An epidemiological study conducted by Metabolic Endocrine Division, Udayana University (2005-2010) obtained the prevalence of DM was 5.9% in Bali.

Meanwhile diabetic retinopathy (DR) is a micro vascular complication of DM. Several studies emphasize the importance role of platelet dysfunction in the pathogenesis of macro vascular and micro vascular complications of DM. Patients with DM with prolonged hyperglycemia conditions will experience platelets dysfunction, in which structural, functional or metabolic changes were occurred. Platelet dysfunction activates the formation of thrombus which is causing embolization of capillary microstructure and attachment of clots to the vascular endothelial including the blood vessels in the retina.

Increasing platelet index values, Mean Platelet Volume (MPV) and PDW indicate the presence of subclinical activation of platelets. Some recent studies have examined the value of MPV and PDW in DM patients and its relationship to the DR staging. The study by Papanas et al, and Kadic et al showed MPV increase significantly in DR condition. Study conducted by Ates et al reported that increasing of MPV values positively associated with DR staging. On the other hand, there was no significant relationship between MPV and PDW against the DR staging. Study conducted by Hekimsoy et al and Jindal et al showed there was no significant difference in MPV values between diabetic patients with DR and without DR. Another study by Citirik et al. obtained there is a significant differences between MPV and PDW in patients with DM, NPDR, and PDR compared with a healthy control group, but none meaningful differences in each staging of DR.

Diabetic retinopathy is still a major cause of vision loss in the productive age. The importance of retinal examination as early as possible to detect retinopathy should be handled early, it caused by the...
high prevalence of diabetes in Indonesia and in Bali. Examination of platelets index as diabetic markers of retinopathy are still debatable. This examination is potential for a simple, easy and inexpensive method to assess the presence of micro vascular complications especially DR in diabetic patients.4,5

Base on the controversial data, researchers want to do a study to assess the relationship between platelet morphology and the staging of DR.

METHOD

This research is an observational analytic study with cross-sectional design to determine the relationship between platelet morphology and staging of DR. This study conducted at Eye Polyclinic Sanglah General Hospital, Bali from April - June 2017. The target population was all DR patients. The study sample was all diabetic patients with retinopathy who came to the Eye Polyclinic of Sanglah Hospital. The samples were taken by consecutive sampling. Data collection is done by interview, physical examination, ophthalmology examination, and blood sampling. All data are analyzed by SPSS 18.0 program. The relationship between platelet morphology (MPV and PDW) with staging of diabetic retinopathy (NPDR and PDR) analyzed by Spearman correlation. Multiple logistic regressions used to analyze the effect of age, sex, duration of DM and hypertension as the control variables.

RESULT

Most of the participants are male 34 (66.7%) and 17 women were included (33.3%). Mean age of the participants was 55.67 ± 8.62 years old. All of the subjects were stayed in Denpasar area as many as 30 people (58%). Onset DM in the sample obtained 12.61 ± 5.11 year. History of hypertension was found in 27 subjects (52.9%). Characteristics of the study samples are shown in Table 1.

Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Descriptive</th>
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</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>34 (66.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>17 (33.3%)</td>
</tr>
<tr>
<td>Age (year) Mean ± SD</td>
<td>55.67 ± 8.62</td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Denpasar area</td>
<td>30 (58%)</td>
</tr>
<tr>
<td>Non-Denpasar area</td>
<td>21 (42%)</td>
</tr>
<tr>
<td>Onset of DM (mean ± SD)</td>
<td>12.61 ± 5.11</td>
</tr>
<tr>
<td>History of Hypertension</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27 (52.9%)</td>
</tr>
<tr>
<td>No</td>
<td>24 (47.1%)</td>
</tr>
</tbody>
</table>

MPV values of each staging of DR can be seen in Table 5. On DR staging, NPDR obtained as many as 14 samples (27.50%) with an average value of MPV was 7.13 ± 1.07 fL, meanwhile in PDR state as many as 37 samples (70.25%) with an average value of MPV was 7.16 ± 1.68 fL.

Analytical test using Spearman test showed insignificant results with correlation coefficient (r) = -0.75 with p value 0.603. Logistic regression test between MPV value and the staging of DR showed there is no association between MPV increase and severity of DR. Value B 0.015, with Odd Ratio (OR) 1.015, 95% confidence interval and p value = 0.944 (table 3). In NPDR state found as many as 14 samples (27.50%) with a mean value of PDW was 19.93 ± 0.92 fL, then in PDR state found as many as 37 samples (70.25%) with the PDW mean value of 20.13 ± 1.31 fL.

Spearman correlation test also showed insignificant result with correlation coefficient (r) = 0.006 with p value 0.967. Logistic regression test between PDW values and staging of DR showed there is no correlation between increasing of PDW value and the staging of DR (Odd Ratio (OR) 1.160; 95% of confidence interval; p value = 0.592). The relationship between MPV, PDW and DR values after controlled with sex, age, onset of DM, and history of hypertension, presented in Table 4 and 5.

After controlled by the control variables of sex, age, onset of DM, history of hypertension, we found MPV value was still not significantly related to staging of DR (OR = 0.986, p = 0.953), the same result was obtained in PDW value (OR = 1.043, p = 0.887).

DISCUSSION

Diabetes mellitus is associated with prothrombotic state lead to both macro and microvascular complications.15,16 The activated platelets are deformed which can be judged from the rise in platelet index values, namely MPV and PDW. This study examined the value of MPV and PDW in 51 samples. Mean of MPV value of 14 samples of NPDR patients were obtained 7.13 ± 1.07 fL, meanwhile mean of MPV value was 7.16 ± 1.68 fL in staging of PDR. There was an increasing of MPV value from NPDR to PDR state, but the results were not statistically significant (p > 0.05). Correlation of MPV with DR staging was analyzed using logistic regression test. It found there is no correlation between increasing MPV value and DR staging progressiveness. Increasing MPV value in vascular disease has been widely studied. The role of MPV in microvascular complication in DM such as retinopathy was still debateable. Tuzcu et al.
investigated MPV values between healthy subjects, subjects with DM without retinopathy, subjects with NPDR, and subjects with PDR. The study showed there are significant differences on the MPV value between healthy subject groups and subject groups with PDR. But the study also found insignificant differences between healthy groups and NPDR group; between NPDR groups and PDR group.

Other studies by Citirik et al° and Yilmaz et al° showed similar results with this study, there were significant differences in MPV value among patients with DM, NPDR, and PDR compared with a healthy control group, but there were no significant differences at each staging of DR. Zhong et al° suggests that MPV may be an independent risk factor of neovascularization. His study showed a significant increasing in MPV value at PDR patients compared with healthy controls. Kadic et al° (2015) examined the value of MPV in patients with type 2 DM. This study showed an increasing of MPV values in patients with poor glycemic control (HbA1C> 7.0%). There is a positive relationship between thrombus formation and HbA1C decline. These findings suggest that platelet activity can be recovered through glycemic status control. The study also found an insignificantly increasing in MPV values in diabetic retinopathy. Increased MPV occurs due to high levels of blood sugar triggers osmotic swelling and shortening of platelet age, indicating MPV could become an indicator of deterioration of glycemic control.

The role of PDW value in diabetic retinopathy has been widely studied. Yilmaz et al° found a significant increasing of PDW value in diabetic patients with retinopathy at all staging. Citirik et al°, found an increasing of PDW in each staging of diabetic retinopathy, but not significant. In this study also found similar result with the studies before. There is an increase in the PDW value of the NPDR group compared with PDR, from 19.93 ± 0.92 fl to 20.13 ± 1.31 fl, but not statistically significant. The study did not consider the use of anti-diabetic drugs. Dolasik et al° mentions the effects of long-term metformin against platelet activation. There is a significant increasing of MPV after the use of metformin for 6 months. The use of insulin as an anti-diabetic drug can also decrease platelet reactivity.

Blood sampling in this study was performed by analyst from the Clinical Pathology Laboratory Sanglah Hospital. Examination of platelet index will be optimal if done within 120 minutes after intake. The limitation of this study were 1) There is no specific standard time applied when collecting and examining the blood samples, the use of EDTA as an anticoagulant for platelet examination is still an option, but it is best checked within 60 minutes before any volume changes and sum. 2) Hypertension is one of the vascular diseases in which atherosclerosis occurs in the blood vessels. Platelet activation also plays role in the pathogenesis of hypertension. This study found no significant results between platelet index and hypertension. 3) This research was conducted at Sanglah Hospital which education Hospital. 4) The sample in this study was taken consecutively, which was not considering the patient’s blood sugar control. Most of the samples got routine treatment to control the blood sugar and blood pressure.
CONCLUSION

Based on the result of this research, it can be concluded that MPV value at Non Proliferative Diabetic Retinopathy (NPDR) is similar with Proliferative Diabetic Retinopathy (PDR). Value of PDW in Non Proliferative Diabetic Retinopathy (NPDR) is not different with PDR. The limitation of this study were platelet index taking and measurement techniques were unstandardized and this study not considering insulin and anti-diabetic drugs used by the subjects. Some studies mention some anti-diabetic drugs can prevent platelet aggregation, so it needs to be investigated further.

CONFLICT OF INTEREST

There are no conflict of interest regards to this article

REFERENCES


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