Introduction

Diabetes Mellitus (DM) is a global health problem with multiple and major complication. Diabetic Foot Ulcer (DFU) is one of those that 15% of diabetic patients experience with DFU during their lifetime. DFU is considered as a major cause of morbidity and hospitalization in diabetics. DFU have multifactorial pathogenesis and a complex several causes; however, the first acting factors are neuropathy and ischemia and occasionally overlapping of these which defined as neuro ischemia.

Mean Platelet Volume (MPV) is a predictive marker of platelet activation and its function. It means that increase of MPV show the synthesis of pro-thrombotic and pro-inflammatory agents in platelets, release of alpha-granules, and release of pretty much reactive platelets from reserves and related with thrombotic disease and atherosclerosis. MPV increases with glucose levels in patients without glycemic control.

Since MPV is an easy and cheap parameter that is strongly correlated with activated platelet and alteration of microvascular circulation and ath-

ABSTRACT

Aims: Diabetes Mellitus (DM) is a global health problem with multiple and major complication. Diabetic foot ulcer (DFU) is one of those that 15% of diabetic patients experience with DFU during their lifetime. Mean platelet volume (MPV) is a marker of platelet activation and function. It means that increase of MPV release of highly reactive platelets from stores and related with thrombotic disease and atherosclerosis. The aim of this study is corresponding elevated MPV on lead to the ulcers.

Methods: We included consecutive 28 patients with Type 2 diabetes and non-gangrenous DFU and matched 28 patients with Type 2 diabetes and without foot ulcers as well as 28 healthy volunteers for age and sex. Diagnostic criteria for diabetic foot ulcers were the presence of systemic signs of infection, purulent wound secretion or at least two local findings of inflammation (e.g., redness, warmth, induration, pain or tenderness).

Results: Hemoglobin level of DFU group was lower than healthy control group (p=0.001). MPV levels were higher in DFU group when compared to diabetic or healthy control groups (p=0.03 and p<0.001, respectively). MPV was higher in diabetic group with DFU when compared to both diabetic and healthy control groups.

Discussion: The atherosclerotic process and disorders of vascular circulation in the course of DFU may explain the high MPV in patients with DFU.

Conclusions: All of these underlying pathogenic disorders may influence the volume of platelets or high MPV -as a marker of more thrombogenic and active platelets- may contribute the development of DFU.

Keywords: Diabetes Mellitus, Diabetic Foot Ulcer, Mean Platelet Volume.

DOI: 10.19193/0393-6384_2017_3_058
erosclerotic factors are main causes in the pathogenesis of DFU, we try to investigate relationship MPV levels with in patients with non-gangrenous DFU. The aim of this study is corresponding elevated MPV on lead to the ulcers.

Material and methods

Since this is a study with human beings, study was carried out according to ethical criteria and to the standards necessary by the Declaration of Helsinki from 1975. This study was confirmed by Harran University Ethics Committee(2012/57) and was only started after the signature of Informed Consent Term.

Our study included consecutive 28 non-gangrenous DFU patients with Type 2 DM, compared 28 patients with Type 2 DM without DFU and 28 healthy volunteers for equal age and sex.

Diagnostic criterias for DFU were the existence of systemic signs of infection, purulent excretion of wound and minimum two regional symptoms of inflammation (e.g., pain, induration, heat, flush or sensitivity). Subjects having Type 1 DM, apparent major organ failure, pregnancy, malignancy, gangrenous foot ulcer (Wagner class 4 and 5), active infection except for DFU and overt cardiac events were excluded. Peripheral artery disease involving in large vessels was excluded by Doppler ultrasound with color in the DFU group. In this study, we studied the patient group with minor vessel injury.

MPV is evaluate in blood samples collected in EDTA tubes, which are analyzed by Abbott Cell-Dyne 4000 cell counter (Abbott®, Abbott Park, North Chicago, Illinois, USA).

Statistical Package for the Social Sciences 20.0 software (for Windows, Chicago, IL, USA) was used for statistical analysis. All data are introduced as mean ± SD and categorical variable factors as percentages. The Kolmogorov-Smirnov test was used to analyze the values distribution. Groups with a normal distribution, were compared with one-way analysis of variance (ANOVA) for variables but groups with anormal distribution, were compared with Mann-Whitney U test for variables. Pearson correlation factor was used for correlation analysis. A two-sided statistically significant p value was take into consideration as <0.05.

Results

Clinically and laboratory data of the three groups were shown in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Healthy group (n=28)</th>
<th>Type 2 DM without DFU (n=28)</th>
<th>DFU patients with Type 2 DM (n=28)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>55.2±8.1</td>
<td>56.1±11.3</td>
<td>53.0±3.8</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>16/11</td>
<td>15/12</td>
<td>14/13</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking (yes/no)</td>
<td>24/4</td>
<td>22/6</td>
<td>21/7</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.2±5.3</td>
<td>28.0±2.9</td>
<td>26.7±2.3</td>
<td>NS</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>118.1±8.0</td>
<td>123.7±15.0</td>
<td>120.3±8.7</td>
<td>NS</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>73.9±8.1</td>
<td>77.4±11.3</td>
<td>75.9±4.1</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.0±0.2</td>
<td>0.9±0.1</td>
<td>0.9±0.1</td>
<td>NS</td>
</tr>
<tr>
<td>FG (mg/dl)</td>
<td>381.4±127.9</td>
<td>303.1±146.8</td>
<td>90.2±7.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>A1c (%)</td>
<td>10.6±2.7</td>
<td>11.0±2.1</td>
<td>-</td>
<td>NS</td>
</tr>
<tr>
<td>WBC (× 10³)</td>
<td>11.1±3.6</td>
<td>9.1±2.7</td>
<td>8.3±2.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10.6±2.7</td>
<td>13.3±1.9</td>
<td>14.0±1.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Platelets (× 10³)</td>
<td>300.1±76.0</td>
<td>295.9±110.9</td>
<td>288.1±66.7</td>
<td>NS</td>
</tr>
<tr>
<td>MPV (fl)</td>
<td>9.4±1.1</td>
<td>8.7±0.9</td>
<td>8.1±1.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 1: Clinical and laboratory data of groups.

A1c, Glycosylated Hemoglobin; NS, Not Significant; FPG, Fasting Plasma Glucose; WBC, White Blood Cell; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MPV, Mean Platelet Volume; BMI, Body Mass Index

Fig. 1: Distribution of the MPV values in studied population.

Age, BMI, gender differences, and systolic and diastolic blood pressures were similar. As expected, glucose levels were higher in both DFU and diabetic control groups than in control group (p<0.001 for all); but, glucose and HbA1c levels were similar in two diabetic groups.
DFU group had higher leukocyte count when results compared with the DM group without foot ulcer and the healthy control group (p=0.32 and p=0.002, respectively). Hemoglobin level of DFU group was lower than healthy control group (p=0.001). MPV levels were higher in DFU group when compared to DM group without foot ulcer or healthy control group (p=0.03 and p=0.001, respectively, Figure 1).

In Pearson correlation analyses, MPV was significantly and positively correlated with only creatinine level (r=0.356, p=0.001).

Discussion

DFU is one of the main complications of diabetes with major morbidities, long hospital stay and high rate of mortalities\(^6\). Foot problems constitute the nearly 20% of hospital admissions of diabetic patients\(^8\). DFU is a complicated problem resulting from the interaction of multiple pathogenic factors like polineuropathy, peripheral vascular disease, trauma and after that infections\(^{10}\). Both macrovascular and microvascular involvement are believed to contribute to the outcomes of vascular disease and bad effect on healing of wound in negative side\(^{10}\).

In generally, large platelets are likely to be young and physiologically active; that means they have more alpha granules, express increased adhesion molecules, produce more thromboxane A2 and showing greater thrombogenic potential when compared with small platelet\(^{12}\). MPV is a part of automatically analyzed complete blood count which reflects the platelet size and is an indicator of platelet reactivity\(^{12}\).

Elevated MPV levels have been reported in diabetic patients\(^{10-11}\). In our study, MPV was trend to increase in diabetic controls but did not reach the significant value. Similarly, Akinsegun et al. found that MPV did not significantly different between diabetics and healthies\(^{12}\).

Furthermore, several studies have shown that increased MPV is related with macro- and microvascular complication of diabetes such as retinopathy, atherosclerosis, microalbuminuria and neuropathy\(^{12,13-15}\).

Recently, Antonopoulos et al. showed that DFU is associated with endothelial dysfunction and increased stiffness of large arteries as a surrogate marker of atherosclerosis\(^{16}\). On the other hand, larger MPV was associated with atherosclerosis and coronary artery disease\(^{17,18}\). We found that MPV was higher in diabetic group with DFU when compared to both diabetic and healthy control groups. The atherosclerotic process and disorders of vascular circulation in the course of DFU may explain the high MPV in patients with DFU.

In our study, apparent artery occlusion defined as Wagner 4 and 5 lesions were excluded. Moreover, we did not classify the DFU as neuropathic, ischemic or mixed lesions. We believe that large and comprehensive studies with well design according to underlying pathological process may display the importance of MPV.

Conclusion

As mentioned above, underlying causes of DFU were multiple and complex including neuropathy, both macro- and micro-vascular circulation defect, inflammation and atherosclerosis. All of these underlying pathogenic disorders may influence the volume of platelets or high MPV -as a marker of more thrombogenic and active platelets- may contribute the development of DFU.

References

9) Thompson CB, Jakubowski JA, Quinn PG, Deykin D,


Authors’ Contributions
AEG carried out the study, sent the manuscript this journal as corresponding author. MD and HK carried out the patients collections. MAE participated in the design of the study and performed the statistical analysis. EYK and TS conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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