The ratio of platelet/lymphocyte, the ratio of neutrophil/lymphocyte and some haemogram parameters related to thrombosis in essential thrombocytosis and polycythaemia vera.

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Abstract

Background: It is known that chronic inflammation plays a role in the mechanisms of thrombosis in PV and ET. The NLR and PLR are chronic inflammatory markers. This study aimed to investigate the relation between NLR, PLR and some hemogram parameters with thrombosis in PV and ET.

Methods: Patient samples were put into Etilendiamin Tetraasetik Asit (EDTA) tubes and were analyzed on the same day in the CELL-DYN3700SL (United States) device. For evaluating the data statistically, the IBM Statistics15.0 (SPSS) statistic package software was used.

Result: A total of 70 patient (26 Prior Thrombosis Event (+) and 44 Prior Thrombosis Event (-)) participated in our study. There was no statistically significant difference in NLR, PLR between patients with and without thrombosis history was determined ($p=0.472$, $p=0.137$).

Conclusion: This study supports that no relationship between levels of NLR, PLR and thrombosis complications in PV and ET. To our knowledge, our study is the first in literature that evaluates the relation between NLR, PLR and thrombosis in PV and ET.

Keywords Policythaemia vera, Essential thrombocytosis, Thrombosis, The ratio of neutrophil/lymphocyte, The ratio of platelet/lymphocyte.

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Introduction

Arterial and venous thrombosis is important causes of morbidity and mortality in Polycythemia Vera (PV) and Essential Thrombocythemia (ET) \cite{1}. The most important factors affecting survival in PV and ET are age, leukocytosis and thrombosis \cite{2}. Thrombotic complications develop in PV at 12-39\% and in ET at 11-35\% \cite{3,4}. In ET and PV, the risk factors for thrombosis include platelet levels, high leucocyte levels and high neutrophil levels. In the recent studies, it was suggested that leucocytosis is a predictive biomarker for thrombotic events \cite{5}. Studies have shown that platelets tend to aggregation spontaneously in PV and ET \cite{6}.

It is known that chronic inflammation plays a role in the mechanisms of thrombosis in PV and ET. The ratio of Neutrophil/Lymphocyte (NLR) is a chronic inflammatory marker. In contrast to other inflammatory markers, NLR is a cheap and easy to obtain marker \cite{7}. It can be used as a marker in predicting cardiovascular events and mortality \cite{8}. The ratio of Platelet/Lymphocyte (PLR) has been shown to be an independent risk factor for chronic inflammation and is more sensitive than NLR \cite{9,10}.

With this retrospective study, we researched the NLR, PLR and some hemogram parameters related to thrombosis in PV and ET.

Methods

Patient samples were put into Etilendiamin Tetraasetik Asit (EDTA) tubes and were analysed on the same day in the CELL-DYN3700SL (United States) device. White blood cell (WBC) was analysed by laser (optical scatter) method. Erythrocytes and thrombocytes were analyzed by flow cytometry. Haemoglobin levels were analyzed by spectrophotometric method.

Statistical analysis

In the analysis of all the data, SPSS (Statistical Package for Social Sciences) for Windows 16.0 statistical software was used. To evaluate the difference between the means of the continuous variables of the 2 groups that don’t distribute normally, the Mann-Whitney U test was conducted. $p<0.05$ was considered statistically significant.
Results

A total of 70 patients [26 Prior Thrombosis Event (+) and 44 Prior Thrombosis Event (-)] participated in our study. The characteristic features are shown on Table 1. The patient group consisted of 44 (%62) ET and 26 (%38) PV.

Table 1. Comparison of some hemogram parameters according to prior thrombosis event in patients.

<table>
<thead>
<tr>
<th>Prior thrombosis event (+)</th>
<th>Prior thrombosis event (-)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient (N)</td>
<td>Median (Min-Max)</td>
<td>Patient (N)</td>
</tr>
<tr>
<td>WBC (K/uL)</td>
<td>26 8.1 (3.5-19.9)</td>
<td>9.6 (5.2-22.0)</td>
</tr>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>26 13.7 (8.2-18.1)</td>
<td>13.9 (7.1-18.9)</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>26 40.1 (24.5-54.5)</td>
<td>40.0 (21.0-58.2)</td>
</tr>
<tr>
<td>Platelet (K/uL)</td>
<td>26 399 (564-869)</td>
<td>483 (164-1369)</td>
</tr>
<tr>
<td>Neutrophil (K/uL)</td>
<td>26 5.6 (1.9-704)</td>
<td>6.3 (3.1-17.9)</td>
</tr>
<tr>
<td>Lymphocytes (K/uL)</td>
<td>26 1.9 (0.8-3.2)</td>
<td>2.1 (0.8-5.4)</td>
</tr>
</tbody>
</table>

*Mann Whitney U Test

The median value of the NLR for patients with prior thrombosis event was 2.6 (1.2-11.2), for patients without prior thrombosis event was 3.1 (1.4-11.3). When comparing the patients with prior thrombosis event to the patients with no prior thrombosis event, it was found that these values showed no statistically significant difference (p=0.472) (Table 2).

Table 2. Comparison of NLR according to prior thrombosis event in patients.

<table>
<thead>
<tr>
<th>Prior thrombosis event</th>
<th>Patient (%)</th>
<th>NLR</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>(Min-Max)</td>
<td></td>
</tr>
<tr>
<td>(+)</td>
<td>26 (37.2%)</td>
<td>2.6 (1.2-11.2)</td>
<td>0.472</td>
</tr>
<tr>
<td>(-)</td>
<td>44 (62.8%)</td>
<td>3.1 (1.4-11.3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>70 (100%)</td>
<td>2.8 (1.2-11.3)</td>
<td></td>
</tr>
</tbody>
</table>

*Mann Whitney U Test

No statistically significant difference was found when NLR and PLR were separately evaluated with prior thrombosis event in PV and ET too (p=0.357, p=0.787, p=0.139, p=0.228).

Discussion

Current risk stratification in PV and ET is designed to estimate the likelihood of recurrent thrombosis: high-risk is defined by the presence of age >60 years or presence of thrombosis history; low-risk is defined by the absence of both of these two risk factors [11]. It is known that chronic inflammation plays a role in the mechanisms of thrombosis in PV and ET. PLR has been shown to be an independent risk factor for chronic inflammation and is more sensitive than NLR [9,10]. NLR, which is calculated from complete blood count with differential, is an inexpensive widely available marker of inflammation. The availability of the NLR has been demonstrated in the risk stratification of patients with various cardiovascular diseases, many kinds of solid tumors, sepsis, and infectious conditions [12-14]. In our study, when the PLR was examined according to the thrombosis history there was no statistically significant difference in the ratio of PLR to thrombosis history (p=0.137). When the NLR was examined according to the thrombosis history there was no statistically significant difference in the ratio of NLR to thrombosis history (p=0.472). This statistical finding was not significant compared to those with chronic inflammation. Because PV and ET are caused by hematopoietic stem cell transformation and is characterized by overproduction of functional blood cells. Therefore, it was thought that this PLR and NLR values would not be meaningful in relation to PV and ET with thrombosis.
The presence of leukocytes above 15 K/uL in patients with PV has been shown by the ECLAP study group to increase myocardial infarction risk [15]. Same results were also reported for patients with ET in different studies [16,17]. In our study, we examined whether leucocyte and neutrophil counts differed according to the thrombosis history in patients. No statistical difference was found (P=0.057, P=0.154). In the conducted studies, it was indicated that the risk of thrombosis increases at a leucocyte count over 11 K/uL [18]. The median value of leucocyte levels in our study was 8.1 K/uL. Therefore, a significant difference was found when compared with the mean platelets haemoglobin and haematocrit thrombosis story and without thrombosis story (p=0.15, p=0.980, p=0.800). The reason that there was no statistical difference was thought to be because the levels at the moment of thrombosis were not used and that the platelets, haemoglobin, haematocrit and leucocyte levels decreased since the patients were included to the study in therapy. The actors involved in thrombosis are vascular endothelial cells, blood cells and coagulation-fibrinolytic system. In particular, endothelial cells are considered to have important role in inflammation and thrombosis [20]. As a member of complex inflammatory system, cytokines interact with inflammation, thrombosis and many other biological reactions [21]. Cytokines, both well (i.e. interleukin family, tumor necrosis factor) and less known (i.e. omentin) are associated with both inflammation and thrombosis. Histopathological assessment revealed elevated tumor necrosis factor-α and interleukin-6 levels in subjects with thrombosis and inflammation [22]. In another report in literature, serum omentin levels were significantly decreased in pregnancy, which is also considered as a prothrombotic state [23]. These cytokines are all expensive markers so their reproducibility is limited. However, hemogram derived markers; such as Mean Platelet Volume (MPV), is by far less expensive than those, and studies reported its association with both inflammation and thrombosis [24]. Our study neutrophil to lymphocyte and platelet to lymphocyte ratios, which could also be associated with thrombosis.

**Conclusion**

With this retrospective study, we researched the NLR, PLR and some hemogram parameters related to thrombosis in PV and ET. It was thought that NLR and PLR could not be used as a thrombosis indicator in this study. Because of this, PV and ET are caused by hematopoietic stem cell transformation and is characterized by overproduction of functional blood cells. In this study, it was thought that some hemogram parameters could not be shown to relate to thrombosis because the patients received treatment.

**References**


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