Evaluation of the Mean Platelet Volume in Children with Juvenile Idiopathic Arthritis

Velat Şen¹, Aydın Ece², Ünal Uluca¹, Ali Güneş¹, İlhan Tan¹, Tuba Tuncel³, Fesih Aktar¹, Buğra Yıldırım¹

ABSTRACT
Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory arthritis in children. Mean platelet volume (MPV) is an indicator of platelet size and has been investigated as an inflammation marker in several diseases. This study was designed to investigate the MPV values in patients with JIA and healthy subjects, and determine the correlation between MPV, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). The hospital records of a total of 40 children with JIA, diagnosed using the International League of Associations for Rheumatology (ILAR) criteria, and 40 healthy controls were enrolled into the study. White blood cell count (WBC), platelet count, CRP, ESR, and MPV levels were retrospectively recorded. Children with JIA had significantly higher MPV values (8.28±1.12 fL) compared to the control group (7.53±1.07 fL) (p=0.003). Significant correlations were found between MPV, ESR, and CRP in the JIA group (r=0.676, p<0.001 and r=0.430, p<0.006). In addition, a negative correlation was found between platelet count and MPV (r= -0.818, p<0.001) in JIA patients. There was no significant difference in WBC values between the patient and the control groups (p>0.05). Our results suggest that MPV levels may be a useful marker of inflammation and prognostic factor for atherosclerosis risk in pediatric JIA patients.

Key words: Children, juvenile idiopathic arthritis, mean platelet volume, inflammation

Jüvenil İdiopatik Artritli Çocuklarda Ortalaña Trombosit Hacminin Değerlendirilmesi

ÖZET
Juvenil idyopatik artrit (JİA) çocuklarda en sık görülen kronik enflamatuar artrittir. Ortalaña trombosit hacmi (OPH) platelet sağılıklığının bir göstergesidir ve çeşitli hastalıklarda bir enfamasyon belirteci olarak arastırılmıştır. Bu çalışma JİA hastalarında ve sağlıklı bireylerde OPH düzeylerini araştırmak ve OPH, C-reaktif protein (CRP) ve eritrosit sedimantasyon hızı (ESR) arastırındaki iliskiyi belirlemek için tasarlanmıştır. Bu çalışmaya Uluslararası Romatoloji Dernekleri Ligi (ILAR) kriterlerine göre JİA tanısı konan 40 çocuğun hastane kayıtları ve 40 sağlıklı kontrol grubu dahil edildi. Beyaz kan hücreleri sayısı (WBC), trombosit sayısı, CRP, ESH ve OPH düzeyleri retrospektif kaydedildi. JİA’lı çocuklarda OPH değerleri (8.28±1.12 fL) kontrol grubuna(7.53±1.07 fL) göre anlamlı derecede yüksek idi (p=0.003). JİA grubunda OPH ile ESR ve CRP arasında anlamlı korelasyon bulunmuştur (r = 0.676, p <0.001 ve r = 0.430, p <0.006). Buna göre, JİA’lı hastalarda OPH ile trombosit sayımı arasında negatif korelasyon bulunmuştur (r = 0.818, p <0.001). Hasta ve kontrol grubu arasında WBC değerleri açısından anlamlı bir fark yoktu (p> 0.05). Bizim sonuçlarımız, pediatric JİA hastalığında OPH düzeylerinin yararlı bir enfamasyon belirteci ve ateroskleroz riski için bir prognotik faktör olabileceği düşündürmektedir.

Anahtar kelimeler: Çocuk, juvenil idyopatik artrit, ortalama trombosit hacmi, enfamasyon

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Correspondence: Velat Şen, Department of Pediatrics, Dicle University Faculty of Medicine, Diyarbakır, Turkey
Tel: +90-412-248 80 01/1074    Fax: +90-412-2488440
Email: drvelatsen@hotmail.com
INTRODUCTION

Juvenile idiopathic arthritis (JIA) is one of the most common pediatric rheumatologic disorders, which is caused by a combination of genetic and environmental factors with an onset before the age of 16 years that lasts for at least 6 weeks (1). All subtypes of JIA are known to be associated with chronic joint inflammation and the elevated concentrations of some biomarkers, such as CRP and ESR may reflect this process. However, ESR can be affected by different factors unrelated to inflammation, including age, renal failure, and anemia. Similarly, CRP shares some of the drawbacks of ESR (2). Rheumatoid inflammation may lead to systemic manifestations, including accelerated atherosclerosis (3). Chronic systemic inflammation with genetic tendency has become widely accepted for its role in the development of atherosclerotic changes. Moreover, reports have underscored the significance of atherosclerosis as a chronic inflammatory disease state of the arteries (4). Since continuous systemic inflammation is known to accelerate atherosclerosis, patients with JIA and especially those with permanent inflammation may be at elevated risk of cardiovascular disease (CVD) (4).

Inflammation is a significant stimulant for platelets. Platelets play an important physiological role in health and disease, as they contribute to hemostasis, inflammation, and the immunity (5). Circulating platelets may vary in size and hemostatic potential. Platelet volume is a marker of platelet function, and the activity is measured using mean platelet volume (MPV) which is a parameter of complete blood count (CBC) analysis, which is generally overlooked by physicians (6). MPV is considered a striking and useful parameter of platelet function and has been investigated as a simple inflammatory marker in several diseases. Some studies have reported that MPV decreases in inflammatory diseases, including ankylosing spondylitis and ulcerative colitis (7,8). However, several studies have demonstrated increased MPV values associated with the increased risk of atherosclerosis, hypertension, myocardial infarction, and coronary heart disease (9,10). Recent reports in the literature have highlighted the growing body of evidence, which defines the important role of MPV in cardiovascular disease (CVD) and in chronic inflammatory disorders (7,10). To the best of our knowledge, there is no data available in the medical literature regarding MPV levels in patients with JIA. Therefore, the aim in this study was to investigate the usefulness of MPV levels in the determination of platelet activation in a group of JIA patients compared to controls.

MATERIALS AND METHODS

Patients

This study was carried out between January and May 2014 on 40 JIA patients (19 boys, 21 girls) that were regularly followed up in the Department of Pediatric Rheumatology of the Dicle University Children’s Hospital. A total of 40 age and gender matched healthy subjects (21 boys, 19 girls) were recruited as the control group. The control group subjects were selected among the children who were undergoing routine checkup with normal physical examination and medical histories. The investigation was performed in a retrospective manner.

The records of the cases with the JIA diagnosis according to the Task Force of the Pediatric Standing Committee of the International League of Associations for Rheumatology (ILAR) criteria were investigated (11). The essential information about the patient with JIA was accessed by investigating hospital records of the patients. Demographic data, weight, height, and age at disease onset were obtained and recorded for each patient. Patients older than 18 years, with other inflammatory, autoimmune, chronic infectious diseases, diabetes mellitus, or chronic renal insufficiency were excluded from the study. In addition, children with a history of cardiac manifestations, valvular heart diseases, or ischemic heart diseases were also excluded.

Biochemical analyses

White blood cell (WBC) count, platelet count, MPV, CRP, and ESR values were recorded using a computerized patient database. Complete blood count parameters of healthy subjects were collected from the same computerized database. The complete blood count analyses were performed using the same analyzer (Abbott CELL-DYN 3700, United States) in the central laboratory of our institution. Standard ethylenediaminetetraacetic acid (EDTA) containing tubes were used for complete blood counts. Ethical approval for the study was obtained from the local ethics committee.

Statistical analysis

Statistical analyses were performed using SPSS (Statistical Package for Social Sciences) version 15.0.
for Windows (SPSS, Inc., Chicago, IL). Numerical variables were expressed as mean ± standard deviation. Categorical variables were expressed as counts and percentages. The Kolmogorov-Smirnov and Shapiro-Wilk tests were performed for continuous variables to check the distribution of normality. Mann Whitney U-test was used for comparison of numerical data of patients and the controls. Chi-square test was used for comparison of nominal or ordinal variables. Spearman correlation analysis was used to examine relationships between numerical variables. A p-value of less than 0.05 was accepted as statistically significant.

RESULTS

A total of 40 patients diagnosed with JIA (21 girls, 19 boys), and 40 healthy controls (19 girls, 21 boys) with the same age range were included in the study. There were no significant differences between patients with JIA and healthy controls in gender distribution (p>0.05). In addition, no significant differences were found between the patients and controls in terms of anthropometric measurements (p>0.05) (Table 1). Mean ages were 10.92±4.40 in the JIA group, and 10.82±4.29 in the healthy control group (p>0.05). The mean age of disease onset in patients was 7.86±3.89 years. The demographic characteristics of the patients and the healthy subjects are listed in Table 1.

Mean ESR and CRP levels of JIA patients were found to be significantly higher than those of the control group (p<0.001 and p<0.001). No significant difference was found in WBC between children with JIA and the controls (p>0.05) (Table 2). However, significantly lower hemoglobin (Hb) values were found in JIA patients compared with the controls (p=0.002). JIA patients had significantly higher mean MPV values compared with the healthy subjects (8.28±1.11 fl, 7.52±1.07 fl, respectively, p=0.003) (Figure 1). Table 2 summarizes the comparison of laboratory parameters in the study population and the control groups. There was significant negative correlation between the mean MPV level and the platelet count in patients with JIA (r= -0.818, p<0.001). This correlation is shown in Figure 2. In addition, the MPV levels had significant positive correlations with ESR and CRP levels (r=0.676, p<0.001 and r=0.430, p<0.006, respectively). The correlation between MPV and CRP in the patient group is shown in Figure 3. However, no significant correlations were found between MPV and WBC levels in the JIA group compared to the healthy controls. There was no statistically significant correlations for MPV compared to age, disease duration, and weight in patients (p>0.05).

DISCUSSION

JIA is one of the most common chronic inflammatory disorders in children. It is a group of rheumatologic diseases, which are thought to affect the synovium and inflammatory cytokines that target structural abnormalities in the joints (1). In patients with JIA, the observation of chronic inflammatory processes have continued to increase over the years with an ongoing subclinical inflammation. Also, the disease has been shown to be a heterogeneous disorder associated with many extra-articular manifestations such as cardiac involvement (12).

ESR and CRP are the biomarkers that reflect the inflammatory response and may offer some inconsistency in reflecting inflammation. They are broadly used to define the acute phase response in rheumotological disorders (13). These markers are clinically applied to the follow-up of JIA patients. Wu et al. reported that both ESR and CRP levels of JIA patients were higher compared to

Table 1. Comparison of demographic and clinical characteristics of the patients and the control group

<table>
<thead>
<tr>
<th></th>
<th>JIA Group (n:40)</th>
<th>Controls (n:40)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>10.9±4.4</td>
<td>10.8±4.3</td>
<td>ns</td>
</tr>
<tr>
<td>Male / Female</td>
<td>19/21</td>
<td>21/19</td>
<td>ns</td>
</tr>
<tr>
<td>Height, cm</td>
<td>139.1±24.5</td>
<td>138.6±24.3</td>
<td>ns</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>37.04±16.1</td>
<td>36.6±15.8</td>
<td>ns</td>
</tr>
<tr>
<td>Age at onset (years)</td>
<td>7.86±3.89</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Data presented as means ± standard deviation, JIA: Juvenile Idiopathic Arthritis
NS: Not significant
Table 2. Comparison of hematological characteristics of JIA and healthy controls [mean±SD]

<table>
<thead>
<tr>
<th></th>
<th>JIA Group (n:40)</th>
<th>Control Group (n:40)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/100 ml)</td>
<td>11.21±1.43</td>
<td>12.26±1.39</td>
<td>0.002</td>
</tr>
<tr>
<td>WBC, /mm³</td>
<td>10.26±3.52</td>
<td>9.66±2.30</td>
<td>ns</td>
</tr>
<tr>
<td>Platelet (x10³ cells/µl)</td>
<td>274.2±104.5</td>
<td>289.4±105.4</td>
<td>ns</td>
</tr>
<tr>
<td>CRP, mg/dl</td>
<td>14.3±8.38</td>
<td>2.79±1.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>31.1±9.6</td>
<td>9.67±3.89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MPV, fL</td>
<td>8.28±1.12</td>
<td>7.53±1.07</td>
<td>0.003</td>
</tr>
</tbody>
</table>

SD: standard deviation, JIA: Juvenile idiopathic arthritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; WBC: white blood cell; MPV: mean platelet volume; NS: Not significant

those of healthy controls (14). This finding is consistent with the results of our study. We also found higher ESR and CRP values in JIA patients compared to the healthy children.

CBC tests are routinely used during the diagnosis and follow-up of inflammatory diseases. MPV, a component of the CBC test, is used as a laboratory marker for measurement of platelet size. Although one of the main functions of platelets is to maintain hemostasis, a previous report demonstrated that platelets play prominent roles in the inflammatory process (15). Activated platelets are important factors for destruction of cartilage in patients with rheumatological diseases. Platelets may influence this status alone or together with other inflammatory cells (16).

Other platelet-derived proteins also play a role in proinflammatory and joint destructive actions (17). Platelets release diverse types and substantial amounts of secretory molecules, including chemokines, and proinflammatory molecules (15).

There are many studies regarding the relationship between MPV levels and increased inflammation in several diseases other than JIA. Therefore, our present study is the first investigation to evaluate the MPV levels in JIA patients. Gasparyan et al. demonstrated significantly increased platelet volume in patients with rheumatoid arthritis (RA) in adults compared to controls (18). However in another study, Kısacık et al. have reported lower MPV values in RA and that the MPV levels increased with treatment (7). Furthermore, various studies have reported that elevated MPV can be regarded as a risk factor in cardiovascular diseases such as myocardial infarction and atherosclerosis (10,15). Our results showed a tendency of elevated platelet activation in JIA as we observed higher MPV levels in JIA patients compared to

![Figure 1](image1.jpg)  
**Figure 1.** Comparison of mean platelet volume between patients with juvenile idiopathic arthritis and the control group (p=0.003)

![Figure 2](image2.jpg)  
**Figure 2.** The correlation between mean platelet volume and platelet count in the patient group (p<0.001)
healthy subjects.

Recently, particular importance was given to the inflammatory aetiology of atherosclerosis. Proinflammatory mediators including IL-6, IL-8, or TNF-α, play an important role in the development and progression of atherosclerotic lesions (3). Also, increased levels of proinflammatory mediators are demonstrated in the course of JIA (19). However, previous studies have reported that MPV is a reflection of prothrombotic conditions, where various inflammatory cytokines such as IL-1, IL-6 and TNF-α regulate thrombopoiesis (20).

Regarding the increased IL-6 and TNF α, we speculate that high MPV levels in JIA may be related to IL-6 and TNF α effect and also activation of platelets. In addition to IL-6 and TNF α, we suggest that these events are promoted by further factors which are not yet known. We propose that together with the inflammatory effects, the elevated MPV values and platelet counts may constitute a tendency for atherosclerosis development.

A negative correlation of platelet count and MPV have been reported in various physiological and pathological situations, reflecting the tendency to ensure haemostasis by protecting a permanent platelet mass. This negative correlation is frequently observed in inflammatory diseases, in which advanced thrombopoiesis increases the circulating platelet counts, and reactive large-sized platelets transmigrate to inflammatory regions (21). Consistent with previous results of studies that investigated different diseases, we found significant negative correlations between mean MPV levels and platelet count in patients with JIA (r= -0.818, p<0.001). In a retrospective study, Yazici et al. found that MPV is correlated with inflammatory markers in patients with RA (22). In the present study, we examined the MPV levels as well as other inflammatory parameters’ such as ESR and CRP levels. We found a significant correlations between MPV, ESR, and CRP values in the patient group with JIA. According to this relationship, we suggest that MPV may be a suitable and useful marker of inflammation.

Some limitations of the study should be considered. One potential limitation is the retrospective study design. In addition, the number of patients with JIA who were investigated was limited. However, this preliminary study sheds light on the use of MPV levels on diagnosing inflammation and the risk of atherosclerosis in JIA. In conclusion, we found significantly higher MPV values in children with JIA compared with the healthy controls. Our results also indicate that platelets may have a role in the systemic inflammatory process of JIA. Therefore, MPV as a simple, routinely used test may be a useful instrument for the evaluation of inflammation, and the CVD risk in children with JIA. Further studies with a larger JIA patient cohort are needed to verify this idea.

Conflict of interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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Mean platelet volume levels in juvenile idiopathic arthritis


