Cardiology in the Young

cambridge.org/cty

Is there any relationship between platelet indices and myocarditis in children?

Damla Geçkalan Soysal[1] and Rahmi Özdemir[2]

[1]Kütahya Health Sciences University, Department of Pediatrics, Kütahya, Turkey and [2]Kütahya Health Sciences University, Department of Pediatric Cardiology, Kütahya, Turkey

Original Article

Cite this article: Geçkalan Soysal D and Özdemir R (2022) Is there any relationship between platelet indices and myocarditis in children? *Cardiology in the Young* **32**: 203–207. doi: 10.1017/S1047951121001773

Received: 9 February 2021
Revised: 18 March 2021
Accepted: 7 April 2021
First published online: 10 May 2021

Keywords:
Myopericardits; platelet indices; children; plateletcrit

Author for correspondence:
Damla Geçkalan Soysal, MD, Department of Pediatrics, Kutahya Health Sciences University Faculty of Medicine, Evliya Çelebi Campus on Tavşanlı Road 10.km Kutahya, Turkey.
Tel:+90-50628443654.
E-mail: damlageckalan@gmail.com

Abstract

Background: Platelet indices are used to evaluate platelet activation and function which change in inflammatory diseases. We hypothesise that platelet indices such as plateletcrit, mean platelet volume, and platelet distribution width may be more useful as prognostic indicators for myopericarditis in children. *Methods:* A total of 60 children were included in this study. Group 1 consists of children with myopericarditis, Group 2 is those with respiratory infections, and Group 3 consists of control group children of similar age and gender with the patient groups. Complete blood count parameters, C-reactive protein, and troponin values of the whole study group were recorded. Myopericarditis was diagnosed based on acute chest pain, dyspnea, palpitations, heart failure signs, arrhythmia symptoms and ST/T wave change, low voltage, supraventricular tachycardia/ventricular tachycardia on ECG, or elevated troponin T/troponin I levels or functional abnormalities on echocardiography. A comparison of the platelet indices made during diagnosis and 2 weeks after treatment was done for the myopericarditis patients. *Results:* There was no statistically significant difference in platelet indicies values. However, the increase in platelets and plateletcrit values after the treatment of myopericarditis was statistically significant. This study pointed out that there was a negative correlation between platelet–plateletcrit values and the troponin I–C-reactive protein. *Conclusion:* We found that platelet count and plateletcrit values increased after treatment. This is important as it is the first study in children to investigate the possible role of platelet indications for myopericarditis in children.

Complete blood count tests are widely used, fast and cheap tests that include various blood cell indices. Platelet indices (platelet count, mean platelet volume, platelet distribution width, and plateletcrit) have been utilised by physicians to diagnose and manage many different medical conditions.[1-4]

Research has shown that platelet indices are affected by bacterial and viral infections, vascular inflammatory diseases, and malignancies. Mean platelet volume, which indicates the platelet size and the response of the bone marrow to infections and inflammation, was the most commonly investigated index.[5-9] Platelets and plateletcrit are effective in inflammation, thrombosis, and cardiovascular pathologies. The plateletcrit actually shows the amount of circulating platelets in a unit volume of blood. As for functionality, it is similar to the haematocrit for erythrocytes.[3-7]

In this study, we aimed to determine the relationship between platelet indices and myopericarditis in a paediatric population. To the best of our knowledge, this is the first study of platelet indices in patients with paediatric myopericarditis in the literature.

Material and methods

We retrospectively analysed the platelet indices of 20 children diagnosed with acute myopericarditis in our hospital within a 5-month period between October 2019 and March 2020. Myopericarditis was diagnosed based on anamnesis, physical examination, cardiac markers, as well as electrocardiographic and echocardiographic evaluations according to the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases.

Diagnosis criteria for myopericarditis

Clinical presentations included acute chest pain, dyspnea, palpitations, signs of heart failure, syncope, and arrhythmia symptoms. Diagnostic criteria included ECG atrioventricular block, ST/T wave change, low voltage, frequent pre-mature beats, supraventricular/ventricular tachycardia and myocardiocytolysis markers, elevated troponin T/troponin I levels, and functional abnormalities on echocardiography. The information regarding diagnostic criteria for suspected myopericarditis was clinically evaluated as ≥1 for clinical presentation and ≥1 for other diagnostic criteria.[10] Patients with a history of viral disease and no other underlying cause for myocardial damage were included in the study with a diagnosis of myopericarditis.

This study included three groups of patients who applied the paediatric emergency department during the time interval of the study. Each group included 20 patients aged between 1 month and 18 years. The complaints of the first and second groups were fever and respiratory symptoms. The first group included patients diagnosed with myopericarditis, the second included the patients who were diagnosed with only respiratory tract infection without myopericarditis. The third control group was chosen cross-sectionally to comprise 20 sex- and age-matched children from the emergency department and the outpatient clinic. Age/gender-appropriate patients who were admitted due to non-infectious and non-inflammatory conditions such as vitamin deficiency and constipation were eliminated from the control group. Patients with bone marrow disease, cancer, immune thrombocytopenic purpura, immunodeficiency diseases, inflammatory bowel disease, and arthritis or who were using drugs to affect the number of platelets were excluded from the study.

All the patients' demographic characteristics, comorbidities, signs, and symptoms were recorded retrospectively. Age, gender, white blood cell count, haemoglobin levels, neutrophil and lymphocyte counts, mean corpuscular volume, red cell distribution width, plateletcrit, mean platelet volume, platelet distribution width, platelet count, C-reactive protein, and troponin values were recorded for the first and second groups. For the third group, all of these parameters, except troponin and C-reactive protein, were recorded. Patients diagnosed with myopericarditis were clinically symptomatic and elevated troponin values were recorded at the time of diagnosis. All patients were treated with intravenous immunoglobulin therapy. After treatment when the patients were clinically asymptomatic and troponin and cardiac echocardiograph controls were normal, they were discharged. Laboratory, electrocardiographic, and echocardiographic findings were recorded in the second week after discharge. This study was approved by the university ethics committee.

Statistical analysis

Statistical Packages for the Social Sciences 18.0 was used for all statistical analyses. Statistically, p-values less than 0.05 were considered significant. The Kolmogorov–Smirnov test was performed on all groups. The Student's t-test was used for tests with parametric distribution and the Mann–Whitney U-test was used for those with non-parametric distribution to examine the differences between the parameters in the groups. Data between multiple groups were compared using the one-way ANOVA test. For determining the relationship between the parameters examined in the groups, the Pearson and Spearman correlation analysis was used. Paired t-test and Wilcoxon signed-rank tests were used to evaluate the parameters before and after the treatment. The ROC analysis was applied to evaluate the sensitivity and specificity of the parameters that were found to be statistically significant.

Results

No statistical difference existed between the groups in terms of age and gender ($p = 0.94$). The median age of patients was 36 months (inter quartile range: 129 months) (2–204 months). The demographic characteristics and laboratory parameters of the study population and control groups at the time of diagnosis are given in Table 1. There was no statistically significant difference between the groups in terms of demographic characteristics and laboratory parameters, except for troponin levels (Table 1). In the myopericarditis patients, two patients who were admitted to the ICU with a diagnosis of fulminant myocarditis and encephalitis died during follow-up. The comparison of the blood test parameters recorded during the diagnosis and after treatment in patients with myocarditis revealed that the platelet count and plateletcrit values were significantly increased after treatment ($p < 0.05$). C-reactive protein and troponin levels were found to be significantly lower after the treatment compared to those during the diagnosis, as was expected. The remaining laboratory parameters were not statistically different during the acute illness and after the treatment (Table 2).

The platelet count–plateletcrit was found to be lower after treatment due to an acute inflammatory process at the time of diagnosis. We also found that there was a strong negative correlation between the platelet–plateletcrit and C-reactive protein–troponin values. There was no statistical difference between mean platelet volume and platelet distribution width values during illness and after treatment (Table 3).

The ROC analysis was performed to predict the occurrence of myopericarditis by the serum platelet and plateletcrit levels. The increase in platelet and plateletcrit values were not found as significant predictors for the occurrence of myopericarditis. Their AUC values were 0.67 (0.50–0.84) and 0.63 (0.45–0.81) with p-values of 0.006 and 0.18, respectively.

Discussion

Our results indicated that platelet count and plateletcrit were suppressed in the active phase of inflammation in children with myopericarditis. In some studies, parameters such as platelet count, leucocyte count, mean platelet volume, and plateletcrit have been used to predict mortality and morbidity in patients with inflammatory diseases.[11-14] Our aim in this study was to reveal platelet index parameters previously found to be statically significant but have never studied in children with myopercaditis that can be used as inflammatory markers.

The data on platelet indices have been accumulating. The negative correlation between platelet count and mean platelet volume is well known. This is thought to reflect the tendency to achieve haemostasis by forming a fixed platelet mass. Mean platelet volume has been studied with regard to diseases such as rheumatoid arthritis, hypertension, diabetes mellitus, Kawasaki disease, acute coronary syndrome, and myocardial infarction.[15-18] Another useful parameter is the plateletcrit, which is used for predicting platelet aggregation and as a marker of cardiovascular disease.[14] Similarly, in the study by Liu et al., 309 Kawasaki patients and 160 healthy controls were analysed to determine whether mean platelet volume and platelet distribution width values have any correlation with coronary artery disease. In that study, patients diagnosed with Kawasaki were found to have a decrease in mean platelet volume and width of platelet distribution as well as an increase in white blood cells, the platelet count, and C-reactive protein.[5] However, in our study, there was no significant difference in platelet indices between myopericarditis and the healthy groups. This result was thought to be due to the limited number of patients.

In terms of the severity of the disease, platelet indices are thought to be a guide in inflammatory conditions before and after treatment. There have been some studies on this subject. In the study of Ozdemir et al. on rheumatic carditis, while the number of leucocytes and platelets was statistically high before treatment, there was no statistically significant difference in mean platelet

https://doi.org/10.1017/S1047951121001773 Published online by Cambridge University Press

Table 1. Baseline characteristics and laboratory parameters of study population and healthy control subjects

Parameters	Group 1(A) Myopericarditis	Group 2 (B) Respiratory tract viral infection	Group 3(C) Control	p-Value A–B	p-Value A–C	p-Value A–B–C
WBC (count/mm^3) (mean ± SD)	7746 ± 3894	8361 ± 2874	9668 ± 1933	0,57	0,055	0,13
Neutrophil count (mean ± SD) (× 10^3 cells/mm3)	3603 ± 1690	4554 ± 2573	3601 ± 1547	0,17	0,99	0,22
Lymphocytes count (mean ± SD) (× 10^3 cells/mm3)	3894 ± 3520	2978 ± 1922	5137 ± 2518	0,31	0,2	0,51
NLR, median-IQR (min–max)	1,24–2,62 (0,18–9,59)	1,9–1,1 (0,23–8,33)	0,63–1,18 (0,22–2,8)	0,24	0,25	0,07
Haemoglobin (g/dl) (mean ± SD)	12,4 ± 1,8	12,9 ± 1,2	13,4 ± 1,6	0,28	0,067	0,12
MCV (fl), median-IQR (min–max)	80,2–11,1 (57–99)	82,8–6,2 (74–94)	82,9–7,3 (71–106)	0,45	0,22	0,40
RDW (%), median-IQR (min–max)	13,6–1,35 (12,4–17,3)	13,1–0,95 (12,5–15,2)	13–1,6 (12,2–17,1)	0,43	0,1	0,21
Platelet count (count10^3/mm^3) (mean ± SD)	274 ± 157	309 ± 124	332 ± 97	0,44	0,16	0,36
MPV (fl) (mean ± SD)	9,2 ± 1,2	8,9 ± 0,9	8,9 ± 1,3	0,46	0,61	0,76
PDW (%) (mean ± SD)	15,9 ± 0,5	15,7 ± 0,3	15,9 ± 0,4	0,14	0,75	2,92
Plateletcrit (%) (mean ± SD)	0,23 ± 0,11	0,26 ± 0,09	0,29 ± 0,09	0,43	0,16	0,25
CRP (mg/l), median-IQR (min–max)	7,3–37 (0,7–138)	4,3–9,5 (0,5–24)	–	0,21	0,055	–
Troponin-I (ng/L), median-IQR (min–max)	186–1390 (70–31,730)	4,5–8,6 (1–19,3)	–	<0,001	0,99	–

Data presented as number (%) and mean ± SD.
CRP = C-reactive protein; IQR = inter quartile range; MCV = mean corpuscular volume; MPV = mean platelet volume; NLR = neutrophil–lymphocyte ratio; PDW = platelet distribution; RDW = red cell distribution width; WBC = white blood cell

Table 2. Distribution of laboratory parameters during diagnosis and after the treatment of patients diagnosed with myopericarditis

Complete blood count	During diagnosis	After treatment	p-Value
WBC (count/mm^3) (Mean ± SD)	7746 ± 3894	9053 ± 2920	0,21
Neutrophil count (× 10^3 cells/mm3) (mean ± SD)	3603 ± 1690	4180 ± 2628	0,42
Lymphocytes count (× 10^3 cells/mm3) (mean ± SD)	3894 ± 3520	4117 ± 2522	0,76
NLR, median-IQR (min–max)	1,24–2,62 (0,18–9,59)	0,96–1,86 (0,09–6,99)	0,94
Haemoglobin (g/dl) (Mean ± SD)	12,4 ± 1,8	12,6 ± 1,2	0,57
MCV (fl), median-IQR (min–max)	80,2–11,1 (57–99)	80,1–8,7 (57,6–97,9)	0,18
RDW (%), median-IQR (min–max)	13,6–1,35 (12,4–17,3)	13,8–1,7 (12,1–16,3)	0,35
Platelet Count (count10^3/mm^3) (mean ± SD)	274 ± 157	360 ± 145	0,04
MPV(fl) (mean ± SD)	9,2 ± 1,2	9,3 ± 1,8	0,79
PDW (%) (mean ± SD)	15,9 ± 0,5	15,5 ± 1,7	0,26
Plateletcrit (%) (mean ± SD)	0,23 ± 0,11	0,30 ± 0,11	0,008
CRP (mg/l), median-IQR (min–max)	7,3–37 (0,7–138)	0,56–1,6 (0,1–6)	<0,001
Troponin-I (ng/L), median-IQR (min–max)	186–1390 (70–31,730)	7–18 (2–141)	<0,001

Data presented as number (%) and mean ± SD
CRP = C-reactive protein; IQR = inter quartile range; MCV = mean corpuscular volume; MPV = mean platelet volume; NLR = neutrophil–lymphocyte ratio; PDW = platelet distribution; RDW = red cell distribution width; WBC = white blood cell

volume and red cell distribution width.[6] In another study, red cell distribution width and platelet values were reported to be high in patients with acute rheumatic carditis, both at the time of diagnosis and after treatment.[16] On the other hand, Zhang et al., in their study on intensive care patients showed that low platelet count, high mean platelet volume, and high platelet distribution width are associated with more serious diseases.[12] In our study, it was found that the number of platelets and plateletcrit values increased after treatment, which was considered statistically significant. No statistically significant difference was found in other platelet index parameters.

In another study evaluating platelet indices as mortality markers in paediatric intensive care patients, mortality was

https://doi.org/10.1017/S1047951121001773 Published online by Cambridge University Press

Table 3. Platelet indicies and correlation analysis in complete blood count of patients with myopericarditis

Parameters	WBC	Lymphocytes	MPV	PDW	CRP	Troponin
Platelet						
r	0,024	0,005	−0,54	−0,52	−0,43	−0,36
p	0,29	0,36	<0,001	<0,001	<0,001	0,02
Plateletcrit						
r	0,27	0,32	−0,31	−0,33	−0,42	−0,37
p	0,031	0,01	0,015	0,009	0,009	0,016

Data presented as number (%) and mean ± SD

r: The Pearson correlation coefficient, *r*, can take a range of values from +1 to −1. A value of 0 indicates that there is no association between the two variables. A value greater than 0 indicates a positive association; that is, as the value of one variable increases, so does the value of the other variable. A value less than 0 indicates a negative association; that is, as the value of one variable increases, the value of the other variable decreases. If this probability is lower than the conventional 5% ($p < 0.05$), then the correlation coefficient is called statistically significant

p: The p-value is the probability that you would have found the current result if the correlation coefficient were in fact 0 (null hypothesis). If this probability is lower than the conventional 5% ($p < 0.05$), then the correlation coefficient is called statistically significant

Data presented as number (%) and mean ± SD

CRP = C-reactive protein; IQR = inter quartile range; MCV = mean corpuscular volume; MPV = mean platelet volume; NLR = neutrophil–lymphocyte ratio; PDW = platelet distribution; RDW = red cell distribution width; WBC = white blood cell

higher in patients with low plateletcrit.[11-14] That study, however, showed that mean platelet volume and platelet distribution width values were not statistically different between the cases and the controls.[11] In fact, mean platelet volume and platelet distribution width values were similar to those found in our study. In our patients with myopericarditis, we detected lower platelet count and plateletcrit values during the acute inflammatory process before treatment. This could be useful in monitoring the disease. A strong negative correlation between platelet–plateletcrit and C-reactive protein–troponin values was also determined.

In our study, according to the ROC analysis, platelets count and plateletcrit values were not found to be predictive of possible myopericarditis. However, the increase in platelet and plateletcrit after treatment was observed to be consistent with clinical improvement. We think that the fact that the predictive value is not significant may be due to the limited number of patients.

Conclusions

To conclude, platelet and plateletcrit values were observed to increase after the treatment of myopericarditis. We found that mean platelet volume and platelet distribution width values were not significant for myopericarditis. We think that it might be useful in the follow-up of the disease, especially in the inflammatory phase suppression of platelet and plateletcrit. In addition, strong negative correlations between platelet count–plateletcrit and troponin were found to be consistent with the literature.

Study limitations

The major limitation of this study is the small sample size of patients. Furthermore, this study is a cross-sectional, single-centre, retrospective study.

Financial support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflict of interest. The authors disclose no conflict of interest.

Ethical standards. This paper did not involve human or animal experimentation.

References

1. Gasparyan AY, Ayvazyan L, Mikhailidis DP et al. Mean platelet volume: A link between thrombosis and inflammation?. Curr Pharm Des 2011; 17: 47–58.
2. Kim HK, Kim JE, Ham CK, Lee DS et al. Prognostic value of platelet indices as determined by ADVIA 120 in patients suspected of having disseminated intravascular coagulation. Int J Lab Hematol 2008; 30: 117–123.
3. Maluf CB, Barreto SM, Vidigal PG. Standardization and reference intervals of platelet volume indices: insight from the Brazilian longitudinal study of adult health (ELSABRASIL). Platelets 2015; 26: 413–420.
4. Bain BJ, Bates I. Basic haematological techniques. In: Lewis SM, Bain BJ, Bates I, (eds). Dacie and Lewis practical haematology. 9th edn. Edinburgh: Churchill Livingstone, 2001: 19–46.
5. Ruixi L, Fang G, Junming H, Qijian Y. Study on the relationship between mean platelet volume and platelet distribution width with coronary artery lesion in children with Kawasaki disease. Platelets 2012; 23: 11–16.
6. Ozdemir R, Karadeniz C, Doksoz O et al. Are mean platelet volume and platelet distribution width useful parameters in children with acute rheumatic carditis?. Pediatr Cardiol 2014; 35: 53–56.
7. Oylumlu, M, Yuksel, M, et al. The usefulness of plateletcrit to predict cardiac syndrome X in patients with normal coronary angiogram. Postepy Kardiol Interwencyjnej 2015; 11: 197–201.
8. Nkambule, BB, Davison, GM, Ipp H. The evaluation of platelet indices and markers of inflammation, coagulation and disease progression in treatment-naïve, asymptomatic HIV-infected individuals. Int J Lab Hematol 2015; 37: 450–458.
9. Mukker, P, Kiran, S, et al. Platelet indices evaluation in patients with dengue fever. Int J Res Med Sci 2018; 6: 2054–2059.
10. Caforio, AL, Pankuweit, S, Arbustini, E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J 2013; 34: 2636–48, 2648a-2648d.
11. Golwala, ZM, Shah, H, Gupta, N, et al. Mean Platelet Volume, Platelet Distribution Width, Platelet Count and Plateletcrit as predictors of in-hospital paediatric mortality: a case-control Study. Afr Health Sci 2016; 16: 356–362.
12. Zhang, S, Cui, YL, Diao, MY, et al. Use of Platelet Indices for Determining Illness Severity and Predicting Prognosis in Critically Ill Patients. Chin Med J (Engl) 2015; 128: 2012–2018.
13. Purbiya, P, Golwala, ZM, Manchanda, A, et al. Platelet Distribution Width to Platelet Count Ratio as an Index of Severity of Illness. Indian J Pediatr 2018; 85: 10–14.
14. Sezgi, C, Taylan, M, Kaya, H, et al. Alterations in platelet count and mean platelet volume as predictors of patient outcome in the respiratory intensive care unit. Clin Respir J 2015; 9: 403–408.

https://doi.org/10.1017/S1047951121001773 Published online by Cambridge University Press

15. Chu, SG, Becker, RC, Berger, PB, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. J Thromb Haemost 2010; 8: 148–156.
16. Kucuk, M, Ozdemir, R, Karadeniz, C, et al. Red blood cell distribution width: can it be a predictive marker for long-term valvular involvement in children with acute rheumatic carditis?. Int J Lab Hematol 2016; 38: 569–575.
17. Mese, T, Guven, B, Yilmazer, MM, et al. Platelet activation markers in children with congenital heart disease associated with pulmonary arterial hypertension. Congenit Heart Dis 2018; 13: 506–511.
18. Efe S, Asker İ, İnal V. Prognostic Significance of Critical Patients' Platelet Indexes in Mixed Type Critical Care Unit. Yoğun Bakım Derg 2019; 10: 13–17.

https://doi.org/10.1017/S1047951121001773 Published online by Cambridge University Press