Evaluation of platelet count, erythrocyte sedimentation rate and C-reactive protein levels in paediatric patients with inflammatory and infectious disease

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Abstract

Inflammatory and infectious diseases are the major causes of morbidity and mortality. The identification of markers for the assessment of disease activity and response to treatment can improve long-term prognosis. The aim of this study was to evaluate platelet count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) among children with inflammatory and infectious disease. This cross-sectional study was conducted in the paediatric immunology and infectious units of Shahid Madani Hospital of Khorramabad. One hundred fifty children, half boys and half girls, with diagnoses of infectious and inflammatory diseases were included in the study. Platelet count, ESR and CRP were measured at the time of hospitalization and thereafter (recovery phase). A questionnaire including demographic information, diagnosis and paraclinical data was completed. At the time of hospitalization, all 150 children had abnormal ESR, 110 (73.3%) had abnormal CRP and 12 (92%) had alterations in platelet count. At the time of discharge, one patient (0.7%) had normal ESR, 132 (88%) had normal CRP and 140 patients (93.3%) had normal platelet count. At the time of discharge, we found a significant difference between the levels of CRP and platelets in girls. This study showed that CRP level is useful during treatment follow-up. Changes in platelet count are likely to be more prevalent in girls.
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Introduction

Inflammatory and infectious diseases are presented with systemic manifestations and are known to be associated with haematologic alterations. They are characterized by immune response to microbial infection, tissue injury and cancer [1] . Biomarkers such as interleukin (IL)-6, IL-8, platelet count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have been considered for the diagnosis of sepsis.

CRP is produced in the acute phase of infection by the liver, and an increase in CRP serum levels is a known diagnostic marker for inflammation and infection [2]. Furthermore, association between platelets and other inflammatory markers, including CRP and IL-6, has been noted during the active phase of infection. ESR and CRP are widely used as clinical markers of inflammation in inpatient and outpatient settings. CRP is useful for diagnosing acute inflammation, especially during acute infection [3]. ESR evaluation, however, is recommended for chronic inflammatory conditions, including bone-associated inflammatory disease. Increased concentration of fibrinogen, clotting factor and alpha globulins during the pathologic states leads to variation in ESR. These markers have been reported to indicate the severity of diseases like rheumatoid arthritis, polymyalgia rheumatica, temporal arteritis and systemic lupus erythematosus [4]. Thrombocytosis (increased platelet count) is reported in children during chronic inflammation, infection,

iron-deficiency anaemia, tissue injury and malignancies [5]. At the site of inflammation, platelet release mediators such as interferon γ, IL-2 and chemokine ligands (CXCL12, CXCL22) elevate the inflammatory process [6]. A number of studies have described an increase in platelet count and reduced mean platelet volume in response to severe infection [7]. Treating the disease normalizes the platelet count and other inflammatory parameters [8−10].

The aim of this study was to investigate the alteration in platelet count, CRP and ESR in children with inflammatory and infectious diseases referred to our centre.

Methods

This cross-sectional study included all children aged 2 to 15 years referred to the paediatric clinic of Shahid Madani Hospital from August to December 2018 who presented with all types of inflammatory and infectious (bacterial or viral) diseases. The time of diagnosis and results of complete blood count, ESR, and CRP tests were recorded.

We excluded from this study patients with haematologic, cardiovascular or bleeding disorders; a history of platelet dysfunction and associated pathologies such as thrombotic thrombocytopenic purpura, platelet release and storage pool defects; diabetes; and disseminated intravascular coagulation.

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Consent to participate from children under 16 years old was provided by a parent or legal guardian.

Improvement in the symptoms was marked as follows: reduction in fever, improvement of clinical symptoms, reduction of ESR and negative culture (if positive at diagnosis).

To measure ESR, anticoagulated blood was made to stand in a vertical column, where red blood cells under the influence of gravity leave the plasma and settle down. The rate of settlement (sedimentation) is measured as the length of column in three stages: 10-minute, 40-minute and 10-minute stages. At the first stage, the sedimentation rate is low, followed by steady and rapid flow in the second stage and an eventual decrease in the final stage. Blood samples were obtained to measure ESR, such that 2 mL of blood was mixed with 5 mL of sodium citrate.

Fresh serum was obtained from centrifuged blood for the measurement of CRP level. CRP was measured by the latex agglutination method, where CRP in blood conjugates with anti-CRP antibody to form agglutination.

Platelet counting was carried out using the Sysmex K-1000 automatic device (Sysmex, Kobe, Japan). Normal ranges were

TABLE 1. Test results of 150 children at admission and at discharge

Test	At admission		At discharge	
	Abnormal	Normal	Abnormal	Normal
ESR	150 (100%)	0	149 (99.3%)	1 (0.7%)
CRP	110 (73.3%)	40 (26.7%)	18 (12%)	132 (88%)
PLT	12 (8%)	138 (92%)	10 (6.7%)	140 (93.3%)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PLT, platelets.

considered as follows: CRP, 1−10 mg/L; platelet, 250<thinsp>3×109/L−450<thinsp>3×109/L; and ESR, 3−13 mm/h. Platelet changes and their correlation with ERS and CRP levels were then determined by statistical analysis. The statistical analysis was performed by SPSS 18 software (IBM, Armonk, NY, USA).

Descriptive statistics were used to describe the data, and the Fisher exact test was used for comparisons. A p value of <0.05 was considered statistically significant.

Results

In our study, 150 children with infectious and inflammatory diseases referred to Shahid Madani Hospital in Khorramabad were enrolled. Half of the patients were male and half female.

At the time of admission, all 150 children presented with abnormal ESR, 110 (73.3%) had elevated CRP levels and 12 (8%) had abnormal platelet levels. At the time of discharge, one patient (0.7%) had normal ESR, 132 (88%) had normal CRP and 40 (93.3%) had normal platelet count (Table 1).

The Fisher exact test showed a significant relationship between platelet and CRP levels at the time of discharge (p < 0.0002). The observed difference was associated with female sex (p < 0.001) (Table 2). The Fisher exact test also revealed a significant relationship between platelet count and CRP at the time of admission (p 0.007). This difference was observed in girls (p < 0.001) (Table 3). No significant correlation was seen between platelet count at discharge and CRP at admission between the two sexes (p 0.063), nor between platelet count at admission and CRP at admission (p 0.119).

No significant relationship between platelet count at discharge and ESR was seen in either of the two sexes (p 0.933). No significant relationship between hospitalization time and ESR was reported (Fisher exact test, p 0.920). Moreover, no significant difference was seen between platelet count at discharge and ESR according to duration of hospitalization. Similar findings were reported for platelet time and ESR.

TABLE 2. Comparison of CRP and PLT in 150 children at time of admission by sex

Sex	CRP	PLT abnormal	PLT normal	Total	p
Male	Normal	1(%1.6)	63(%98.4)	64	0.853
	Abnormal	0	11 (%100)	11	
Female	Normal	4(%5.9)	64(%94.1)	68	<0.001
	Abnormal	5(%71.4)	2(%28.6)	7	
Total	Normal	5(%3.8)	127(%96.2)	132	0.002
	Abnormal	5(%27.8)	13(%72.2)	18	

CRP, C-reactive protein; PLT, platelets.

Discussion

The present study was performed of 150 children referred to Shahid Madani Hospital, Khorramabad, who presented with infectious and inflammatory diseases. The purpose of our research was to investigate the role of platelet count, ESR and CRP in inflammatory and infectious diseases in the paediatric population. We found a significant relationship between platelet count and CRP at the time of discharge in the girls in our study population. No such differences were found otherwise.

CRP and ESR are commonly used markers to determine the severity of infection. Furthermore, elevation of CRP levels corresponds to an increase in acute inflammatory response. Increase in platelet count is associated with an increase in the activity of bone marrow cells mediated by the production of IL-1 and IL-6 (inflammatory cytokines) [11–13]. A study by Milovanovic et al. [3] reported that IL-6, CRP and platelet counts mark the inflammatory states and are correlated with each other.

Zareifar et al. [14] conducted a cross-sectional study of 100 children diagnosed with inflammatory and infectious disease at a hospital in Shiraz, Iran. Results reported that the patients at the time of admission had increased platelet count compared to the time of discharge. ESR was significantly reduced at the time of admission. The study concluded that platelet count and ESR can be considered effective markers to examine disease activity.

Unkila-Kallio et al. [15] reported that among paediatric patients with haematogenous osteomyelitis, CRP and ESR

levels are elevated and normalize with treatment. They indicated that white blood cell count is a poor indicator for diagnosing the disease and measuring treatment efficacy. Vermeire et al. [16] also reported that CRP is a useful marker in Crohn disease and can also help determine the need for a colectomy, because it indicates the severity of the inflammation. Furthermore, the role of platelets during inflammatory and infectious diseases has also been accounted in a number of studies. Platelets have been found to secrete inflammatory factors, such as histamine, serotonin, p-selectin, CD40L, platelet-derived growth factor, platelet microbicidal proteins and β-defensin, which play a significant role in immunity during sepsis [17]. Al Shibli et al. [18] reported that among children with bronchiolitis, elevation in platelet count (thrombocytosis) is a common presentation; however, it is not associated with disease severity or complications. On the contrary, sepsis is also defined as a critical thrombocytopenic disease in a number of studies [19]. Imani-Rastabi et al. [20], studying haematologic parameters for the diagnosis of sepsis, reported an increase in CRP and ESR and a reduction in platelet count during the disease's infectious stage.

Studies have reported alterations in the size, shape and number of platelets in patients with inflammatory bowel disease. The mean platelet count reduces significantly and is inversely related with ESR and CRP levels. Variations in the platelet count might be seen, depending on the type of the disease (ulcerative colitis or Crohn disease) [21]. The findings of our study parallel those presented by Jeschke et al. [22], indicating that CRP levels are significantly higher in girls than in boys in cases of infection and inflammation.

Our study included a broad range of patients, and given that the pathogeneses of different infectious and inflammatory disease may vary, clinically relevant conclusions could not be drawn. However, one of the important findings from our study is the difference in clinical biomarkers of inflammation and infections between the two sexes. CRP and ESR levels cannot be measured at the same instant. CRP levels increase during bacterial infection and decrease in response to viral invasion [4]. Hence, our study suffers from limitations that do not permit us to draw clinical conclusions from our findings, but that can direct the course of future hypotheses and studies.

Conclusion

CRP levels and platelet counts were high in patients at the time of referral and at discharge. With improvement in patient health, CRP and platelet levels were significantly reduced. Nonetheless, variations in the levels of ESR were seen. Furthermore, our results showed significant correlation

TABLE 3. Comparison of CRP and PLT in 150 children at time of discharge by sex

Sex	CRP	PLT abnormal	PLT normal	Total	p
Male	Normal	62(%96.9)	2(%3.1)	64	0.726
	Abnormal	11(%100)	0	11	
Female	Normal	63(%92.6)	5(%7.4)	68	<0.001
	Abnormal	2(%28.6)	5(%71.4)	7	
Total	Normal	7(%5.3)	125(%94.7)	132	0.007
	Abnormal	5(%27.8)	13(%72.2)	18	

CRP, C-reactive protein; PLT, platelets.

between CRP and platelet levels in girls. Overcoming the limitations of our study can help researchers and clinicians obtain precise results.

Conflict of interest

The authors deny any conflict of interest in any terms or by any means during the study.

Financial Disclosure

The remaining author have no financial relationships relevant to this article to disclose.

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