THE ROLE OF PLATELET-TO-LYMPHOCYTE RATIO IN THE DIAGNOSIS OF INFECTIOUS MONONUCLEOSIS

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ABSTRACT

Introduction: We investigated the use of Platelet-to-Lymphocyte Ratio (PLR) which can be calculated by using platelet and lymphocyte counts from total blood count, for the diagnosis of infectious mononucleosis (IM).
Materials and methods: Out of 116 patients, 24 of them were diagnosed as IM with regard to serological tests and accepted as patient group. 40 healthy subjects were taken as control group. PLR values of the patient and control groups were calculated and cutoff values were determined using ROC Curve analysis.
Results: According to the study data, sensitivity and specificity of PLR value in diagnosing IM is 50% and 95%, respectively.
Conclusion: We concluded that low values of PLR can be used to give an idea about the existence of IM. However, high values of PLR may necessitate more evaluation for other differential diagnosis.

Keywords: Infectious Mononucleosis, Epstein-Barr Virus, Platelet, Lymphocyte.

Introduction

Epstein-Barr virus (EBV) is a common infectious agent, found in approximately 95% of the world's population. Infection with EBV which leads to infectious mononucleosis (IM) is more frequent during childhood[1].

Diagnosis of IM is based on clinical examination, revealing the classic triad of fever, lymphadenopathy, and pharyngitis, and laboratory findings including the presence of atypical lymphocytosis, heterophile antibodies and EBV spesific antibodies. The disease is managed specifically with supportive care since it is a self-limited infection. However, IM has been associated with numerous early or late complications[2].

Various markers are used for the diagnosis of the diseases. Most recently, the use of Platelet-to-Lymphocyte Ratio (PLR) has captivated the attention of researchers. PLR seem to be effective to estimate prognosis for most types of cancer like prostate, ovarium or colorectal cancer. Apart from cancer types, there are studies showing that PLR can be used for early diagnosis of diseases like diabetes mellitus, celiac disease and vestibular neuritis[3-6].

In recent years, there are numerous researches showing that Neutrophil-to-Lymphocyte Ratio (NLR) and PLR are significant markers for diagnosis and prognosis. However, any study on the relation between PLR and IM disease has not found.

This research is planned to examine how PLR of people diagnosed as EBV positive differs.

Methods

116 patients who were admitted to the pediatric clinic of TOBB ETU Hospital between January 2005 - March 2015 and in the age range of 0-15 years were investigated. Complete blood counts and EBV antibodies used for the diagnosis of infectious mononucleosis of these patients were analysed on the day they were admitted to the hospital.

Complete blood count was analysed using Sysmex XT2000i (Sysmex Co., Japan), C-reactive protein (CRP) and ferritin levels using Cobas 6000 (Roche Diagnostics Co., Mannheim, Germany) and EBV IgM (Anti-VCA (Viral capsid antigen) GP 125 IgM, anti-VCA P19 IgM, anti EBNA-1 (EBV Nuclear Antigen) IgM, anti P22 IgM and anti-EA-D (Early Antijen) IgM antibodies) using Euroline Anti-EBV Profile 2-IgM (Euroimmun Medizinische Labordiagnostika AG, Lübeck, Germany).

Patients are diagnosed as IM if they were positive for EBV Anti-VCA G IgM and anti-EA IgM antibodies 24 patients out of 116 were diagnosed as IM regarding to this condition.

Control group was formed from 40 patients between the ages 1 and 15 who were admitted to the pediatric clinic of TOBB ETU Hospital in March 2015. İn order to exclude anemia or infection, ferritin value above 20 ng/ml, leukocyte count under 10 x 103/μl and CRP level under 5 mg/L were taken as inclusion criteria for the control group. Normal reference ranges for each parameter are shown in Table 1.

	Normal Reference Ranges				
CRP (mg/L)	0-5				
Ferritin (ng/ml)	7-140				
Leukocyte	*1 month-1 year*	*1 - 3 year*	*3-5 year*	*5-12 year*	*12-15 year*
(10 x 103/ml)	5-19,5	6-17,5	5,5-15,5	4,5-13,5	4,5-11,0

Table 1: Normal Reference Ranges.

PLR values are calculated by analysing the blood counts of both groups using the formula:

PLR = Platelet Number / Lymphocyte Number.

Mean, median and standart deviation values (SD) are calculated individually for four groups,

namely all the patients who underwent infectious mononucleosis IgM scan, only the seropositives, only the sero negatives, and the control group) (Table 2).

| Platelet-Lymphocyte Ratio		
	n	*mean±SD*
Total scanned group	116	112±70
IM + Group	24	71±55
IM – Group	92	123±70
Control Group	40	82±23

Table 2: PLR values of the patients in the study and the subgroups.

The cutoff values were identified by using ROC curve analysis. According to these cutoff values, percentages of the groups were compared by chi-square test and Odds Ratio was calculated. All statistical calculations were performed by using commercially available statistical software package (SPSS 18, Chicago, IL, USA).

Results

24 patients are found to be EBV positive out of 116 patients who were included in the study (20,7%). The average PLR value of these patients was 112±70. Whereas, 67 out of 116 patients' average PLR value was below 112 (%57.7), Out of these 67, 19 of them were diagnosed as EBV positive.

ROC curve analysis was carried out by using PLR values of 24 IM positive patients and of 40 patients in the control group (Figure 1). Cutoff value for PLR is assessed as 48 considering the specifity and sensitivity values (Table 3).
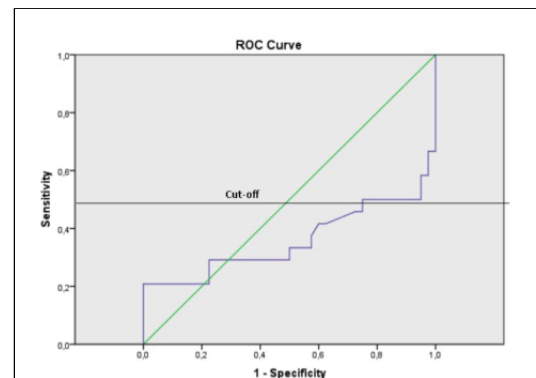
Fig 1: ROC Curve Analysis.

When cuttoff value for PLR was taken as 48, sensitivity and specifity were found to be 50% and 95%, respectively. Positive predictive value (12/14) and negative predictive value (38/50) for IM were found to be 85,7% and 76%, respectively (p<0,001).

	IM + (n, %)	Control (n, %)	Total (n, %)
PLR less than 48	12	2	14
	85,7%	14,3%	100%
PLR more than 48	12	38	50
	24,0%	76,0%	100%
Total	24	40	64
	37,5%	62,5%	100,0%

Table 3: Distributing the patients regarding PLR values.

Discussion

Infectious mononucleosis is a lymphoproliferative disease caused by EBV and generally seen in pediatric population. Laboratory tests have an important role in the diagnosis and follow-up of IM. Although heterophile antibodies can help the diagnosis, measurement of specific antibodies to EBV is the gold standard test for IM. However, tests detecting EBV antibodies are expensive, time consuming, and sometimes hard to reach. Thereby, new tests which are economic and easy to use are needed.

There are various laboratory analyses for the differential diagnosis of diseases. Lately, it is reported that Trombocyte-Leukocyte Ratio can be used in different diseases.

Akboğa et al. investigated the relationship between PLR value and inflammation and the severity of coronary atherosclerosis. They categorized 1646 patients according to Gensini scores as control, mild, and severe coronary artery disease (CAD) groups. They found that PLR values of the patients in the control group is lower than the others and discovered a correlation between PLR and the severity of CAD. They suggested that PLR can be used as a fast and cheap inflammation marker[3].

Furthermore, Langsenlehner et al. researched the usage of PLR as a prognostic indicator for prostate cancer by using the data of 374 patients. When the cutoff value for PLR is set as 190, they saw that an increased PLR is a significant prognostic factor for poor metastases-free survival, cancer-specific survival and overall survival. Based on this finding, they concluded that PLR may predict prognosis in patients with prostate cancer and can contribute to individual risk assessment in them[4].

Kemal et al. reported that Neutrophil to Lymphocyte Ratio (NLR) and PLR can be used in the diagnosis of lung cancer (LC) and studied the NLR and PLR values of 81 LC patients and 81 healthy subjects. They showed that PLR and NLR values of LC patients are higher than the control group and suggested that NLR and PLR can be useful biomarkers in LC patients before treatment[5].

Chung JH et al investigated whether PLR and NLR values are significant markers for vestibular neuritis disease. They showed that PLR and NLR values of the patient group is higher compared to the control group. They also showed that NLR and PLR value of patients with nystagmus ongoing more than five days were significantly higher than that of patients whose nystagmus ceased within five days. They concluded that these two values can be used as a reliable parameter for predicting the cause and severity of the disease[6].

Moreover, it was reported that high PLR may indicate a worse prognosis in some certain diseases like Behçet's Syndrome, brucella arthritis, infective endocarditis, colorectal cancer, coronary artery ectasia and Henoch-Schonlein Purpura[7-12].

Surprisingly, PLR value of IM positive group is lower than the controls in our study group. 85,7% of patients whose PLR value were under the cutoff value were EBV positive and 95% of patients who were IM negative has a PLR above the cutoff value. Regarding these observations it can be claimed that decreased PLR values may be useful in the diagnosis of IM.

Out of 116 patients with prediagnosis of IM, only 24 (20,7 %) of them were antibody positive. However, in our group with lower PLR, the positivity rate of antibodies is 85,7%. So, roughly we can interprete that PLR can be used as a pre-test for IM. It can save us from nearly 65% of unnecessary tests especially in local regions in which measuring specific antibodies is not possible.

Conclusion

According to our data, as a pretest for IM low values of PLR can be used to have an idea about the existence of IM before the results of advanced spesific serological tests. However, high values may indicate the necessity of a new point of view for the differential diagnosis.

On the other hand, the results that we obtained from a limited number of cases, need to be confirmed in wider case series.

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