

Platelet Count and Mean Platelet Volume: Supportive Markers in Differentiation of Tuberculosis and Sarcoidosis

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ABSTRACT

Background and Objectives: Tuberculosis and sarcoidosis are two diseases showing histological and clinical similarities and differential diagnosis of two is still very challenging. Platelet count PLT and MPV are new inflammatory markers investigated in different chronic diseases. But their role in differentiation of tuberculosis and sarcoidosis is not well known. In present study we aimed to assess platelet count (PLT) and mean platelet volume (MPV) as supportive markers in distinction of sarcoidosis and tuberculosis.

Patients and Methods: 100 patients with sarcoidosis, 83 patients with tuberculosis and 36 healthy subjects were included in this retrospective study. Subject's characteristics, leukocyte (WBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), PLT and MPV values were recorded.

Results: Eligible 219 patients were enrolled in present study. CRP, ESR, WBC and PLT values were found higher in tuberculosis patients than that of sarcoidosis and control patients. PLT was significantly higher and MPV was lower in tuberculosis group compared to sarcoidosis group. The most appropriate cut-off value of PLT and MPV to distinguish tuberculosis from sarcoidosis was determined as 300.000 and 8,5 respectively. PLT value above 300.000 and MPV value below 8,5 were found meaningful to differentiate tuberculosis from sarcoidosis.

Conclusion: PLT and MPV were found to be supportive markers in differentiation of tuberculosis and sarcoidosis.

Keywords: Mean platelet volume, platelet, sarcoidosis, tuberculosis

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BACKGROUND

Platelets (PLT) play a crucial role in antimicrobial host defenses and the coagulation system (1). It is known that thrombocytosis exists in tuberculosis and increase in thrombocyte count correlated with severity of disease (2). There is also a significant correlation between the degree of thrombocytosis and acute phase reactants as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) in pulmonary tuberculosis (3-4). The mean platelet volume (MPV) reflects the size of platelets and correlate with function and activation of platelets (5-6). The importance of MPV has been emphasized as an inflammation marker in some chronic inflammatory diseases and inverse correlation between disease activity and MPV has been demonstrated (7-10).

Tuberculosis and sarcoidosis are both granulomatous diseases and can present with similar symptomatology (11). Because the differential diagnosis of tuberculosis and sarcoidosis is difficult, new markers for differentiation are being investigated (12).

PLT and MPV values in sarcoidosis were not well studied. The research of this study is to determine whether PLT and MPV can be used as a differential marker between sarcoidosis and tuberculosis.

METHODS

A retrospective observational cohort study was conducted at a chest disease and thoracic surgery teaching and research hospital. This study protocol was approved by the institution's ethics committee and was in accordance with the Declaration of Helsinki.

Patients with sarcoidosis (group 1, n:100), patients with tuberculosis (group 2, n:83), and healthy subjects (group 3, n:36) were included in the study. Data was collected from the

hospital records between January 1, 2010 and November 1, 2014. Patients' characteristics, smoking habits, hemogram parameters including PLT and MPV, sedimentation and CRP levels on admission were recorded.

Histopathologically granulomas with no caseification was found in all patients who are compatible with sarcoidosis as clinically and radiologically in the group 1 accepted as sarcoidosis. Sputum AFB (with Ziehl-Neelsen stain) and at least one culture (Löwenstein-Jensen media and BACTEC TB 460 system) were found positive in all patients in the group 2, accepted as lung tuberculosis. Normal healthy individuals presenting for routine examination with no complaint or known disease with a normal chest radiography were accepted as control patients in the group 3.

The exclusion criteria were, haematological disease, hepatic and renal or autoimmune disorders, cardiovascular disease, systemic arterial hypertension, endocrinological disorders, cancer and immunosuppressive conditions. None of the enrolled subjects had received anticoagulant medications, NSAID or contraceptives (11-12).

Full blood counts were carried out using Beckman Coulter haematologanalyser (Tokyo-Japan), ESR (eritrocyte sedimentation rate) with Alifax ESR analyser (Polverara-Italy) and serum levels of CRP (C-Reactive Protein) with Garnet-Siemens (Germany) devices in all groups.

Statistical Analysis

Statistical analysis were performed using NCSS (Number Cruncher Statistical System) 2007 & PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) program. Data were analyzed using descriptive statistical methods (mean, standard deviation, median, frequency, rate, minimum, maximum). Student's t test was used for the comparison of quantitative variables of two groups with normal distribution. Oneway Anova test was used in

comparison of three groups with normal distribution and Tukey HSD test and Tamhane test was used in the determination of the group that cause differences. Kruskal-Wallis test was used in comparison of three groups with non- normal distribution and Mann-Whitney U test was used in the determination of the group that cause differences. In the comparison of qualitative data Pearson Chi-square test was used. Significance was considered at $p < 0.01$ and $p < 0.05$ values.

RESULTS

Eligible 219 patients were included in the study. The ages of the patients ranged from 18 to 80 , mean age was 45.17 ± 18.66 years. Women constituted 79% of the sarcoidosis patients and female gender ratio of sarcoidosis group was significantly higher than the tuberculosis and control group ($p < 0.001$). Demographic characteristics of patients were shown in Table 1 (Table 1).

ESR and CRP values were lowest in the control group ($p < 0.01$ and $p < 0.01$). ESR and CRP values in sarcoidosis patients were lower than tuberculosis patients (respectively $p < 0.01$ and $p < 0.01$). Leukocyte (WBC) values were significantly lower in control and sarcoidosis patients than tuberculosis patients ($p < 0.06$ and $p < 0.001$ respectively). There was found no significant difference between control group and sarcoidosis group in terms of ESR, CRP and WBC levels ($p > 0.05$). PLT count of sarcoidosis patients was significantly lower than that of tuberculosis patients ($p < 0.001$). PLT count of the patients in the control group were also significantly lower compared to the TB group ($p < 0.001$). Between sarcoidosis and control groups, there was no statistically significant difference in terms of PLT count ($p > 0.05$) . MPV measurements of tuberculosis cases were found significantly

lower than the sarcoidosis and control group ($p < 0.001$, $p < 0.010$ respectively). MPV value was not differ significantly between sarcoidosis and control groups ($p > 0.05$). ESR, CRP, WBC, PLT and MPV values of the groups were shown in Table 2 (Table 2).

Because PLT and MPV values of tuberculosis and sarcoidosis groups were found significantly different, it was considered to be calculated the most appropriate cut-off values in differential diagnosis of two diseases. In determining the cut-off points of PLT and MPV, diagnostic screening tests and ROC analysis were used.

In this study, the most appropriate cut-off value of PLT was determined as 300.000 to distinguish tuberculosis from sarcoidosis. For this cut-off value it was found to be sensitivity as 53.01 % ; specificity as 72.73 % ; positive predictive value as 61.97 % and negative predictive value as 64.86 % (Figure 1-2).

The best MPV cut-off value in differential diagnosis of tuberculosis and sarcoidosis was defined as 8,5. For this cut-off value for the diagnosis of tuberculosis sensitivity was found as 73,49 % ; specificity as 68,04 % ; positive predictive value as 66,30 % and negative predictive value as 75,00 % (Figure 3-4).

DISCUSSION

Differential diagnosis of tuberculosis and sarcoidosis is still important issue because they can mimic each other as in symptomatology, both are granulomatous diseases pathologically but treatment of each disease was different (11). Our findings provide novel information related to new biomarkers for differentiating tuberculosis and sarcoidosis. In tuberculosis, CRP, ESR, WBC and PLT was found significantly higher than sarcoidosis. MPV was inversely correlated with inflammation and it was lower in tuberculosis patients. $PLT > 300.000$ and $MPV < 8.5$ values contribute to differentiate tuberculosis from sarcoidosis.

In most of the infectious and chronic inflammatory diseases, reactive thrombocytosis can be seen as a systemic inflammatory response. In pneumonia, platelet response in antimicrobial host defense is similar to the leucocyte response and thrombocytosis should be considered as a poor clinical outcomes (1). CRP is an acute-phase reactant secreted from hepatocytes in response to tissue damage or inflammation. The ESR, another acute phase reactant, has been found to be high in patients pneumonia and tuberculosis (13). Robson et al defined severe pulmonary tuberculosis characterised immunologically by an acute phase response (14). Reactive thrombocytosis developing in pulmonary tuberculosis has been shown to be correlated with acute phase reactants and severity of the disease (15,16).

In this study CRP,ESR,WBC and PLT were found higher in tuberculosis than in sarcoidosis and control groups. PLT was significantly higher in tuberculosis patients compared to sarcoidosis. In the comparison of tuberculosis and sarcoidosis, a cut-off value off PLT > 300.000 can differentiate tuberculosis from sarcoidosis with 73% specificity.

MPV has attracted attention as a new inflammatory marker because it can be easily measured in routine complete blood count analysis, it's quick and cheap. MPV reflects platelet size and function and the size of platelets in circulation is affected by intensity of inflammation (9). The size of platelets decrease and smaller platelets released from bone marrow with overproduction of proinflammatory cytokines and acute phase reactants, so low MPV can be explained in this way (5). MPV has been investigated in different chronic diseases and inverse correlation with inflammation has been demonstrated (7-10).

However MPV is a little known marker for differentiating sarcoidosis and tuberculosis. In the studies related to MPV in tuberculosis, MPV has been shown lower in active tuberculosis patients than control group (4,17). But in some studies MPV was found significantly higher in active tuberculosis patients and decreased with antituberculosis

treatment (2,16). In present study MPV values of tuberculosis patients were significantly lower than that of sarcoidosis and control group. In Dirican et al's study MPV values was not differ significantly between sarcoidosis and control groups (18). Also in this study, MPV was similar in sarcoidosis and control groups but it was found significantly lower in tuberculosis group other than two groups. In the comparison of tuberculosis and sarcoidosis, a cut-off value off $MPV < 8,5$ can differiante tuberculosis from sarcoidosis with 68% specificity.

Limitations of present study are being retrospective, conducted in a single centre, based on hospital archive. Nevertheless, the results from disese-specific study population studied at the largest chest disese teaching and research hospital in the region provide valuable clinic information for assesing PLT and MPV as new inflammatory biomarkers in differiantiation of tuberculosis and sarcoidosis.

CONCLUSION

Differential diagnosis of tuberculosis and sarcoidosis are still very challenging. PLT and MPV are new inflammatory markers investigated as supportive markers for distinguishing two diseases. In present study PLT and MPV was found significantly different between tuberculosis and sarcoidosis groups. $PLT > 300.000$ and $MPV < 8,5$ values support the diagnosis of tuberculosis . Our findings support the idea that PLT and MPV could be used as a supportive marker for differiantion of tuberculosis from sarcoidosis. Future studies can be planned to clarify the utility of these markers in distinction of tuberculosis and sarcoidosis.

Declaration of interest statement

None of the authors have any conflict of interest.

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Table 1: Patients characteristics

Groups	n	Age Year±SD	Gender	
			Male n (%)	Female n (%)
¹ Sarcoidosis	100	45,16±11,90	21 (21,0)	79 (79,0)
² Tuberculosis	83	40,70±20,15	61 (73,5)	22 (26,5)
³ Control	36	36,75±14,62	16 (44,4)	20 (55,6)
<i>p</i> 0,001**			0,001**	

Table 2: Laboratory findings of three groups

Groups	ESR	CRP	WBC	PLT	MPV
	mean±SD	mean±SD	mean±SD	mean±SD	mean±SD
¹ Sarcoidosis n:100	39,11±27,62	12,44±16,21	7,36±2,13	262,49±68,61	8,93±0,94
² Tuberculosis n:83	78,88±41,70	52,71±48,49	9,20±2,98	323,87±96,64	8,15±0,94
³ Control n:36	14,11±11,05	4,33±2,80	7,61±1,98	252,69±81,49	8,77±0,85
<i>p</i>	0,001**	0,001**	0,001**	0,001**	0,001**
1-2	0,001**	0,001**	0,001**	0,001**	0,001**
1-3	0,001**	0,007**	0,987	0,988	0,848
2-3	0,001**	0,001**	0,006**	0,001**	0,010*

ESR:Erythrocyte sedimentation rate, CRP: C-reactive protein, WBC: White blood cell count

PLT:Platelet count, MPV: Mean platelet volume

** $p < 0,01$

* $p < 0,05$

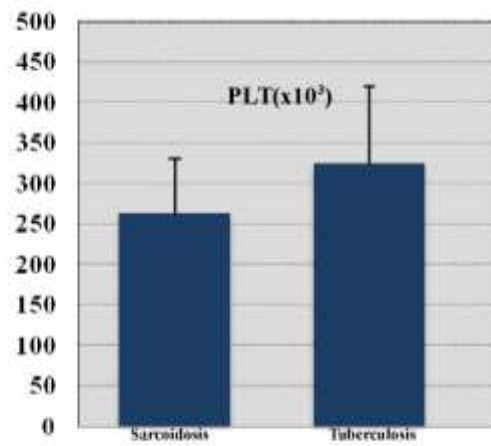


Figure 1: Distribution of PLT values according to groups

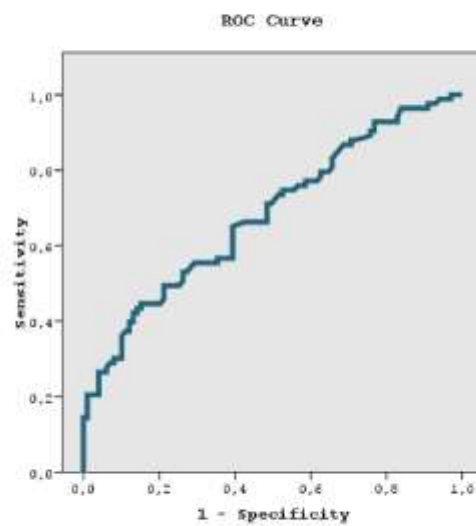


Figure 2: ROC curve for using PLT levels in tuberculosis

The area below the ROC curve was found to be 68.1 % and the standard error was 4.0 %.

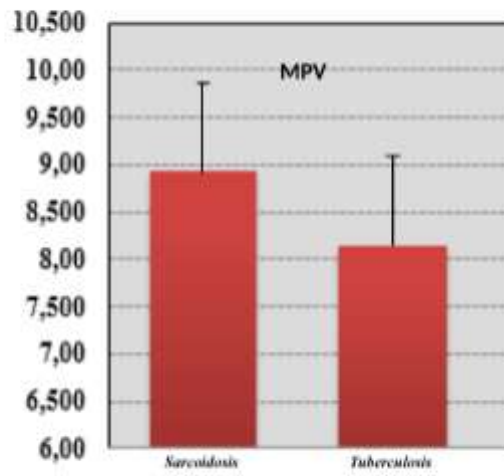


Figure 3: Distribution of MPV values according to groups

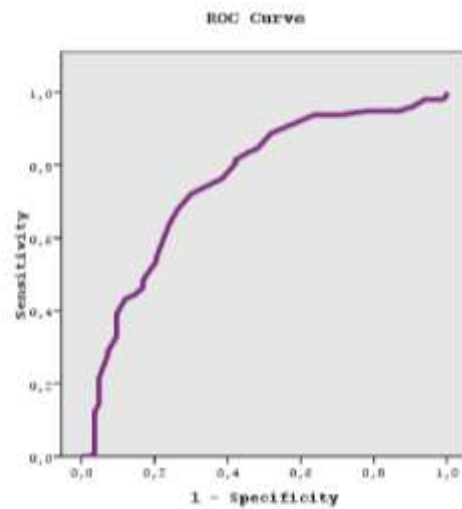


Figure 4: ROC curve for using MPV levels in tuberculosis

The area below the ROC curve was found to be 75,4 % and the standard error was 3,7 % .