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Platelet lymphocyte ratio, lymphocyte monocyte ratio, mean platelet volume, and neutrophil lymphocyte ratio in Behcet's disease and their relation to disease activity

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Abstract

Background: Behcet's disease (BD) does not have specific laboratory finding or pathological physical examination sign, and only few studies have investigated Neutrophil to lymphocyte ratio (NLR), platelets to lymphocytes ratio (PLR), lymphocytes to monocytes ratio (LMR), or mean platelet volume (MPV) values in patients with BD. We conducted this study to investigate the relationship between these indices and Behcet's disease (BD) and to determine their relation to BD disease activity.

Results: This study is a case-control study that included 36 Behcet's disease patients and 36 healthy controls. BD patients showed significant increase in the mean of NLR and PLR in comparison to control ($P = 0.008$ and 0.011) respectively, and highly significant decrease in LMR and MPV levels in BD patients in comparison to control ($P < 0.001$ and < 0.001) respectively. Also, we found that NLR, PLR, and LMR were significantly related to BD activity, and there were significant associations between the studied hematological parameters with some of muco-cutaneous, articular, gastrointestinal, eye, and nervous system manifestations in BD patients.

Conclusion: The blood indices NLR, PLR, LMR, and MPV are potential inflammatory markers that can be used to evaluate inflammatory status and disease activity in patients with BD. NLR and PLR showed positive relation being higher in active disease and also higher in highly active disease than in low disease activity. Also, LMR was significantly decreased in Behcet's disease patients in relation to disease activity. Furthermore, NLR and PLR levels were significantly more associated with muco-cutaneous and nervous system involvement while, LMR levels were significantly associated with muco-cutaneous, articular, gastrointestinal and eye manifestations and MPV levels were associated with articular manifestations being significantly related to disease activity. These easily evaluated markers could help in the management of this disease with multisystem affection that are sometimes serious and potentially life threatening.

Keywords: Behcet's disease, NLR, PLR, LMR, MPV

Background

Behcet's disease (BD) is a relapsing autoimmune disorder, characterized by recurrent oral and genital ulcers, ocular lesions, and different systemic manifestations [1]. Behcet's disease does not have a pathological physical examination sign and there is a lack of a universally recognized pathognomonic test [2], but many markers were

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suggested as associated with BD such as tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), interleukin 1 beta (IL-1β), vascular endothelial growth factor (VEGF), thrombomodulin E-selectin, total homocysteine, α-2 macroglobulin, and α-1 antitrypsin [3–5].

Platelet lymphocyte ratio (PLR), Neutrophil lymphocyte ratio (NLR), and mean platelet volume (MPV) were suggested as indicators of systemic inflammation in numerous researches [4, 6]. The inflammatory process in BD entails inflammatory cells and molecules that alters the size, shape, and number of peripheral blood cells. Neutrophils are involved in the production of inflammatory cytokines, which result in the activation of neutrophils [7]. During this process, dysregulation in the control of lymphocytes apoptosis may lead to decrease in the production of lymphocyte [8].

Neutrophil lymphocyte ratio (NLR) can be calculated by leukocyte subgroup of complete blood count and its ratios, it has been widely used to define the severity of inflammation and endothelial activation in many diseases as BD, autoinflammatory diseases, hypertension, diabetes mellitus, and malignancies [9–14].

Platelet to lymphocyte ratio (PLR) is also a biomarker that denotes the existence of inflammation [6]. PLR is like NLR and unlike other inflammatory biomarkers is a cheap marker calculated from complete blood count and it has been studied in many inflammatory conditions like rheumatoid arthritis and systemic lupus erythematosus and in malignancies [15–17].

Mean platelet volume (MPV) is detected in complete blood count, it represents the mean size of the thrombocytes and is indirectly associated with the activity of platelets [9, 18, 19]. Compared to small platelets, large platelets have more dense granules than small platelets. Prothrombotic factors as serotonin, thromboxane A2, β-thromboglobulin, and ATP are released from these granules, which have an impact on the inflammatory process and endothelial functions. Also, they contribute to the expression of adhesion factors including P-selectin and glycoprotein IIb/IIIa, which result in an increase in vasoconstriction [20, 21].

Lymphocyte monocyte ratio (LMR) was first defined as a biomarker for infectious disease and a reflection of the balance between effector and host [5]. It has been shown that TNF-a, IL-1, IL-6, and IL-8 are elevated in the sera of patients with BD. Although many immunologically active cells and neutrophils may produce these cytokines due to stimulation, monocytes are one of the major sources of some of these cytokines. Therefore, it is not surprising to find activated monocytes in patients with BD [22].

Elevated levels of different inflammatory markers have been found in BD including ESR, CRP, peripheral leukocyte and platelet counts, and serum cytokines [23–26]. Of which, ESR and CRP are often used for evaluating BD activity [27]. However, they are not specific for BD as they can be affected by several physiologic and pathologic conditions [28].

To the best of our knowledge, few studies have investigated NLR, PLR, LMR, and MPV values in patients with BD. Therefore, to better understand these serum inflammatory parameters in BD and to gain deeper insight into their role in BD, we conducted this study to assess these indices in BD and evaluate their association with the disease activity and some of the clinical manifestations of BD.

Methods

Patients and controls

This case-control study included 72 participants, 36 BD patients and 36 apparently healthy persons as control matched for age and sex. Patients were recruited from the outpatient clinic of Department of Rheumatology, Rehabilitation and Physical Medicine, Assiut University, Egypt, during the period from December 2018 to April 2019. We included patients older than 18 years old, with Behcet's disease diagnosed by a rheumatologist according to the International Criteria for Behcet's Disease (ICBD) [29].

Patients with hematological disorders, impaired coagulation tests, hyperlipidemia, hypertension, peripheral or coronary artery disease, abnormal hepatic or renal function tests, diabetes mellitus, autoimmune disease other than BD, active infectious disease or malignant diseases, and patients who were using aspirin and other platelet active drugs, steroids, or immunosuppressive drugs during the previous 6 months were excluded from the study.

Clinical and laboratory profile

All patients were subjected to detailed history including demographic data and detailed clinical history (disease duration, symptoms, and medications such as DMARDs, prednisone, biologics). Also, full general and rheumatological examinations were done.

All BD patients were classified as active or inactive groups according to the simplified Behcet's Disease Current Activity Form (BDCAF), which record clinical manifestations during the 4 weeks prior to the assessment. It includes 12 items (headache, mouth ulceration, genital ulceration, erythema, skin pustules, arthralgia, arthritis, nausea/vomiting/abdominal pain, diarrhea + altered frank blood per rectum, eye involvement, nervous system involvement, and major vessel involvement) the score is graded from 0 to 12 and active disease was defined with BDCAF ≥ 2 [30–32].

Laboratory analysis included complete blood count (CBC) with differential white blood cell count, CRP,

and ESR. Blood samples were collected in vacuum tubes with EDTA as anticoagulant for automated CBC including differential cell count that was measured by Hematology Analyzer ADVIA 2120i (Siemens Healthcare). ADVIA 1800 Chemistry Analyzer with the capability of the immunoturbidimetric assay was used for CRP. CUBE 30 TOUCH (Siemens Healthcare) fully automated system was used for ESR analysis (mixing and reading), the results provide excellent correlation to the 1-h Westergren reference method.

Assessment of NLR was done by dividing the absolute neutrophil count on the absolute lymphocyte count, assessment of PLR was done by dividing the platelet count on the absolute lymphocyte count, assessment of LMR by dividing the absolute monocyte count on the absolute lymphocyte count. MPV was also detected.

There were three primary end points which were first, to determine PLR, LMR, MPV, and NLR levels in BD patients; second, to assess their relation to BD activity; and third, to assess their relation to BD clinical manifestations.

All procedures performed were in accordance with the ethical standards of the Assiut University Medical Ethical Review Board (IRB no. 17100568) and with the 1964 Helsinki declaration ethical standards.

Statistical analysis

All statistical calculations were performed using statistical package for the social science, version 22 (SPSS, Chicago, IL, USA). Quantitative variables were described in the form of mean ± standard deviation (SD) when normally distributed and median (range) when not normally distributed. Qualitative variables were described as number and percent. Mann-Whitney *U* test was used for comparison of non-normally distributed quantitative variables. Qualitative variables were analysed using $\chi 2$ (chi square) test or Fisher's exact test when the expected frequency is less than 5. *P* value≤0.05 is considered significant.

Results

Both BD patients and control groups were compared regarding baseline socio-demographic data and there were no statistically significant differences between them (Table 1).

The clinical manifestations of the studied BD patients group include muco-cutaneous involvement (e.g., mouth ulceration, genital ulceration, skin pustules, erythema nodosum, superficial thrombophlebitis) that was present in 22 (61.1%) patients, articular involvement (e.g., arthralgia, arthritis) in 20 (55.6%), gastrointestinal involvement (e.g., nausea, vomiting, abdominal pain, diarrhea with blood per rectum) in 4 (11.1%), eye involvement (e.g., red eye, blurred vision, painful eye) in 28 (77.8%) patients, Nervous system involvement (e.g., headache, blackout, difficult speech, difficult hearing, double vision, lost sensation at Face, arms, or legs, memory loss, loss of balance) in 32 (88.9%) patients, and major vessels involvement (e.g., chest pain, hard breathing, cough of blood, pain, swelling or discolouration of the face, arm, or leg) in 4 (11.1%) patients (Fig. 1).

Table 1 Comparison between studied groups as regards age and sex

	Patients ($N = 36$)		Control ($N = 36$)		*P value*
Age (years), mean ± SD	35.9 ± 8.2		33.9 ± 8.8		0.360
Sex, *n* (%)					
Male	32	(88.9)	27	(75.0)	0.126
Female	4	(11.1)	9	(25.0)	

Quantitative data are expressed as mean ± SD and range; qualitative data are expressed as *n* (%)

* Significance defined by $p \leq 0.05$

NLR, PLR, ESR, and CRP levels across the two study groups where statistically significantly different, with BD patients having higher levels of these parameters than healthy controls ($P < 0.05$); Meanwhile the control group had higher levels of LMR and MPV than BD patients ($P < 0.001$) (Table 2).

Furthermore, by comparing the above-mentioned parameters among active and inactive BD patients we found statistically significant differences between both studied groups as regards NLR, PLR, LMR, ESR, and CRP ($p < 0.05$), where active BD patients had higher NLR, PLR, ESR, and CRP, and lower level of LMR than inactive BD patients. Meanwhile there was no statistically significant difference between active and inactive BD patients as regards MPV (Table 3).

Then by comparing BD patients according to BD activity index, we found that, patients with higher BD activity index (> 3) have statistically significant higher NLR and PLR ($P = 0.001$ and 0.027) respectively, and statistically significant lower LMR level than in patients with low BD activity index (2–3) ($P = 0.001$). There was no significant difference in MPV levels in relation to degrees of BD activity (Table 4).

Regarding the relation of the studied hematological indices with the clinical manifestations of BD, we observed that patients with muco-cutaneous involvement have significantly higher NLR, PLR, CRP, and significantly lower LMR compared to patients without muco-cutaneous involvement. Patients presented with articular involvement have significantly lower MPV compared to patients without articular involvement. Patients presented with

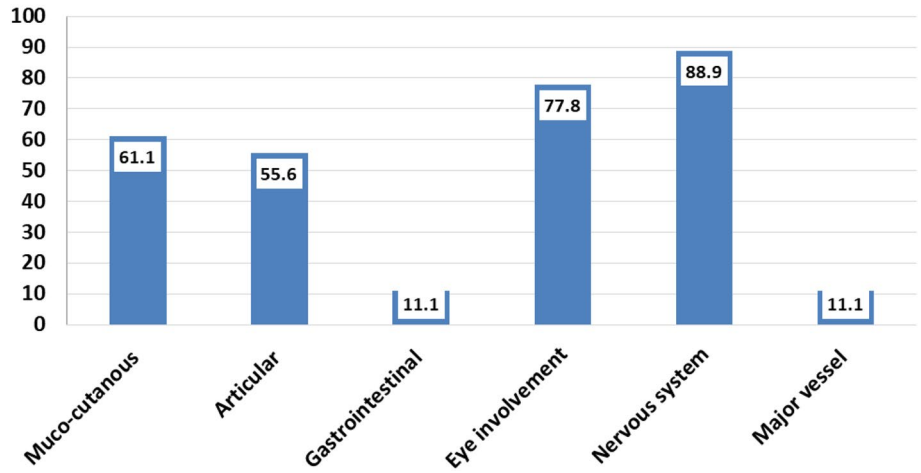

Fig. 1 Bar graph showing the incidence of different clinical manifestations among the studied cases. Data are represented as %

Table 2 Comparison between patients and control groups as regard studied laboratory data

Laboratory data	Patients ($N = 36$) Median (range)	Control ($N = 36$) Median (range)	*P value*
➢ NLR	3.5 (0.4–9.6)	1.7 (0.8–9.8)	0.008*
➢ PLR	12.1 (4.2–27.3)	8.0 (3.8–51.0)	0.011*
➢ LMR	0.09 (0.01–0.30)	0.2 (0.08–0.82)	< 0.001*
➢ MPV	8.0 (6.4–9.4)	11.0 (9.0–13.7)	< 0.001*
➢ ESR (mm/h)	30.0 (9.0–141.0)	12.0 (7.0–15.0)	< 0.001*
➢ CRP (mg/L)	3.2 (1.09–60.0)	0.3 (0.3–0.3)	< 0.001*

NLR Neutrophil lymphocyte ratio, *PLR* Platelet to lymphocyte ratio, *LMR* Lymphocytes to monocytes ratio, *MPV* Mean platelet volume, *ESR* Erythrocyte sedimentation rate, *CRP* C-reactive protein. Quantitative data are expressed as median (range)

* Significance defined by $p \leq 0.05$

Table 3 Comparison between active and inactive BD patients as regards studied laboratory data

Laboratory data	Behcet's disease activity		*P value*
	Active ($n = 18$) Median (range)	Inactive ($n = 18$) Median (range)	
➢ NLR	3.8 (1.0–5.4)	1.8 (0.4–9.6)	0.009*
➢ PLR	13.7 (6.6–18.9)	9.9 (4.2–27.3)	0.047*
➢ LMR	0.08 (0.01–0.30)	0.11 (0.07–0.25)	0.013*
➢ MPV	8.3 (6.4–9.3)	7.7 (6.8–9.4)	0.501
➢ ESR (mm/h)	55.5 (9.0–141.0)	28.0 (10.0–60.0)	0.010
➢ CRP (mg/L)	13.2 (1.09–60.0)	2.7 (1.2–14.5)	0.034

NLR Neutrophil lymphocyte ratio, *PLR* Platelet to lymphocyte ratio, *LMR* Lymphocytes to monocytes ratio, *MPV* Mean platelet volume, *ESR* Erythrocyte sedimentation rate, *CRP* C-reactive protein. Quantitative data are expressed as median (range)

* Significance defined by $p \leq 0.05$

Table 4 Comparisons of studied laboratory data as regards Behcet's activity index

Laboratory data	Behcet's disease activity index		*P value*
	2–3 ($n = 22$) Median (range)	> 3 ($n = 14$) Median (range)	
➢ NLR	1.8 (0.4–9.6)	4.1 (3.4–5.4)	< 0.001*
➢ PLR	9.9 (4.2–27.3)	13.3 (8.7–18.9)	0.027*
➢ LMR	0.13 (0.03–0.30)	0.08 (0.01–0.11)	0.001*
➢ MPV	8.3 (6.8–9.4)	7.9 (6.4–9.0)	0.102
➢ ESR (mm/h)	28 (10–110)	36 (9–141)	0.240
➢ CRP (mg/L)	2.7 (1.2–60.0)	13.2 (1.09–38.3)	0.191

NLR Neutrophil lymphocyte ratio, *PLR* Platelet to lymphocyte ratio, *LMR* Lymphocytes to monocytes ratio, *MPV* Mean platelet volume, *ESR* Erythrocyte sedimentation rate, *CRP* C-reactive protein. Quantitative data are expressed as median (range)

* Significance defined by $p \leq 0.05$

gastrointestinal involvement have significantly lower LMR compared to patients without gastrointestinal involvement. Patients with eye involvement have significantly higher LR compared to patients without eye involvement. Patients with nervous system involvement have significantly higher NLR and PLR compared to patients without this involvement. And finally, patients with major vessel involvement have no significant relation with any of the studied hematological indices (Table 5).

Discussion

Behcet's disease (BD) is a systemic vasculitis disease that is characterized by recurring attacks of oral ulcers, genital sores, and ocular lesions (triple-symptom

Table 5 The relation between the clinical presentations of BD patients and the studied laboratory data ($n = 36$)

Clinical presentation	NLR	PLR	LMR	MPV	ESR	CRP
Muco-cutaneous involvement						
• No	1.80 (0.77–9.60)*	9.90 (6.60–27.30)*	0.13 (0.07–0.25)*	7.7 (6.8–9.4)	28.0 (10.0–110.0)	2.67 (1.20–3.50)*
• Yes	3.80 (0.40–5.40)	13.30 (4.20–18.90)	0.08 (0.01–0.30)	8.3 (6.4–9.3)	36.0 (9.0–141.0)	13.20 (1.09–60.0)
Articular involvement						
• No	3.80 (0.40–9.60)	14.70 (4.20–27.30)	0.09 (0.03–0.30)	9.1 (6.4–9.4)*	36.0 (9.0–141.0)	7.73 (1.60–60.0)
• Yes	2.60 (1.00–4.70)	9.90 (6.60–15.50)	0.10 (0.01–0.18)	7.7 (7.3–9.0)	28.0 (10.0–131.0)	2.67 (1.09–24.0)
Gastrointestinal involvement						
• No	2.60 (0.40–9.60)	10.90 (4.20–27.30)	0.10 (0.01–0.30)*	8.1 (6.4–9.4)	29.5 (9.0–141.0)	3.11 (1.20–60.0)
• Yes	4.15 (3.70–4.70)	12.70 (8.70–13.20)	0.06 (0.05–0.09)	7.7 (7.3–8.3)	30.0 (19.0–118.0)	14.50 (1.09–23.09)
Eye involvement						
• No	3.75 (0.40–5.40)	12.85 (4.20–13.30)	0.08 (0.01–0.09)*	8.3 (7.3–9.2)	27.5 (9.0–131.0)	6.73 (1.50–14.50)
• Yes	2.60 (0.77–9.60)	9.90 (6.60–27.30)	0.10 (0.03–0.30)	7.8 (6.4–9.4)	36.0 (10.0–141.0)	3.16 (1.09–60.0)
Nervous system involvement						
• No	1.14 (0.77–1.50)*	8.25 (7.30–9.20)*	0.14 (0.03–0.25)	7.9 (6.8–9.1)	65.0 (60.0–100.0)	31.56 (3.11–60.0)
• Yes	3.70 (0.40–9.60)	12.85 (4.20–27.30)	0.09 (0.01–0.30)	8.0 (6.4–9.4)	28.0 (9.0–141.0	2.94 (1.09–38.30)
Major vessel involvement						
• No	2.60 (0.40–9.60)	9.90 (4.20–27.30)	0.10 (0.03–0.30)	8.0 (6.4–9.4)	28.0 (9.0–141.0)	3.11 (1.09–60.00)
• Yes	3.80 (3.70–4.20)	13.25 (13.20–13.30)	0.08 (0.01–0.09)	8.0 (7.3–9.0)	30.5 (30.0–131.0)	13.00 (1.50–14.50)

NLR Neutrophil lymphocyte ratio, *PLR* Platelet to lymphocyte ratio, *LMR* Lymphocytes to monocytes ratio, *MPV* Mean platelet volume, *ESR* Erythrocyte sedimentation rate, *CRP* C-reactive protein. Quantitative data are expressed as median (range)

* Significance defined by $p \leq 0.05$

complex). While the exact pathogenesis of Behcet's disease is still not known, neutrophil hyperfunction, vasculitis, and autoimmune response seems to be responsible for the disease. Until now, there is no particular serum biomarker or diagnostic test for BD [4, 33, 34].

Our study demonstrated that NLR and PLR were higher in Behcet's patients in comparison to control ($P = 0.008$ and 0.011) respectively. In accordance with our results were Gheita et al. [31], Öztürk et al. [5], Balkarli et al. [27], and Alan et al. [15] who reported significantly higher NLR in BD patients versus controls, suggesting that neutrophil hyperactivity leading to innate immune system dysfunction has an important role in BD pathogenesis [24, 25].

We also found that both NLR and PLR were significantly greater in active BD patients compared to inactive patients ($P = 0.009$ and 0.047) respectively and were increased in high disease activity group than in low disease activity group ($P = 0.001$ and 0.027) respectively. These results are in agreement with Öztürk et al. and Balta et al., who reported that in active BD patients the levels of NLR was significantly greater compared to inactive patients. The fact that inflammatory cytokines lead to increased neutrophil production in active BD, as part of the inflammatory process can explain the rise in NLR [5, 35].

Moreover, Öztürk et al. reported that, the NLR could predict the BD activity and was related to endothelial dysfunction, also, they found that NLR was correlated positively with CRP which was in line with our study [5].

Also, Yuksel et al. [14] found that NLR was increased in active BD in comparison to the inactive BD and controls and in relation to the activity of ocular involvement in BD patients, which supported the prospect that neutrophils were activated in BD and affected the inflammatory cascade of BD [36].

In 2015, Alan et al. reported the relation between PLR and the presence and activity of BD, they classified BD patients according to disease activity into mild, moderate, and severe and indicated that compared to healthy controls, BD patients' PLR and NLR levels were significantly higher, but they found no association between the BD activity score and PLR, NLR, and MPV [37], that was unlike our findings in which the BD activity was positively related to PLR and NLR, while negatively related to LMR and not significantly related to MPV.

Our results were supported by the study of Jiang et al., who found significantly higher levels of PLR and NLR in BD patients versus controls, also they found significantly higher PLR and NLR in active versus inactive BD patients [28].

Numerous studies reported that high PLR and low LMR were associated with disease activity in many

diseases, but they could not show these correlations with other inflammatory markers such as hs-CRP or ESR [38–42].

Regarding LMR, we found that it was lower in BD patients compared to controls ($P = 0.001$) and lower in active BD patients compared to inactive BD patients ($P = 0.013$), also it was lower in patients with high BD activity index (> 3) than patients with low BD activity index (2–3) ($P = 0.001$).

In agreement with our results were Jiang et al, who found significantly lower levels of LMR and MPV in BD patients versus controls, but their results differ than ours in the finding that there was insignificant difference in LMR levels between active and inactive patients [28].

In a study done by Wang et al. they studied the LMR ratio in active tuberculosis patients, after anti-tuberculous therapy and in controls. They found that LMR was predictive for active tuberculosis and that it might be considered a systemic inflammatory marker to monitor tuberculosis progress and treatment [43]. Furthermore, Du et al. reported low LMR in patients with ulcerative colitis and a positive correlation with the disease activity [44].

These findings support our results in which decreased LMR along with decreased lymphocytes and increased monocytes in patients compared to healthy controls and in association with increased BD activity, indicate deterioration of lymphocyte/monocyte-mediated immunity. These results agree with other studies denoting lymphopenia as a common complication that increase the infection risk in autoimmune diseases [45, 46].

Lymphocyte count decrease in peripheral blood might be caused by persistent accumulation of lymphocytes at the sites of inflammation and might result from apoptotic markers increase in peripheral blood lymphocytes of patients [47]. So, an abnormal LMR might reflect systemic inflammation and the severity of immune injury.

The present study demonstrated that MPV level was lower in BD patients thanin controls ($P < 0.001$). In accordance with our result, the study of Lee and Kim [48], who reported that the MPV was decreased in BD than in controls.

We also found that there was no significant difference of MPV values between active and inactive BD and there was no significant relation between BD activity score and MPV. These results were in accordance with the studies of Balkarli et al., Jiang et al. and Alan et al. [27, 28, 37].

There were many studies regarding MPV in BD, but the association between BD and MPV levels has been demonstrated in them with conflicting results [21, 48]. Açıkgöz et al. found that MPV was significantly increased in BD patients in comparison to controls and was correlated with increased tendency to develop thrombosis, but between individuals with active and inactive BD, MPV levels did not significantly differ [21]. An explanation for this discrepancy was the possibility that MPV alone was not an appropriate indicator of platelet activation. In agreement with this explanation was a conclusion stated by Beyan et al., who concluded that, platelet indices such as MPV should not be used alone as direct indicators of platelet activation, as they found no correlation between platelet aggregation responses and platelet indices [49].

In a study done by Yolbas et al., they reported that MPV levels were slightly elevated in BD patients and lower in active BD patients in comparison to the inactive patients. This discrepancy between MPV levels in inflammatory disorders could be explained by variations in patients' disease activity status and current therapies. Additionally, the anticoagulants chosen for blood samples and the intervals between blood sample collection and analysis can affect MPV levels [50].

In our study, we found that NLR and PLR were significantly higher in association with muco-cutaneous and nervous system involvement and had no significant relation to other studied BD manifestations. Another finding was that LMR was significantly lower in association with muco-cutaneous and gastrointestinal manifestations and was significantly higher in association with eye manifestations. MPV was significantly lower in association with articular manifestations. We found no significant relation between the studied laboratory parameters and major vessels involvement.

In agreement with our results was the study by Lee and Song, they found that although NLR was higher in patients with active BD compared to those with inactive BD, it was not significantly higher in patients with thrombotic BD compared to those without thrombosis, and patients with active BD did not have significantly different MPV than those with inactive BD, or between those with thrombosis and those without it [51]. Also, Balkarli et al. found that MPV values were similar when compared groups of active BD with or without thrombosis [27].

In contrast to our results were Alan et al., who demonstrated that NLR, PLR, and MPV were not associated with BD involvement in the joints, eyes, nervous system, major vessels, or gastrointestinal tract [37], and Açıkgöz et al., who found that MPV was associated with an increased tendency to develop thrombosis [21]. Also, Öztürk et al., Balkarli et al., and Ünlü and Arslan, reported a positive correlation between NLR and endothelial dysfunction in BD patients [5, 27, 52].

Another contradicting study to our results is Gheita et al., who reported that NLR and PLR were significantly higher in BD patients with vascular manifestations than in those without vascular manifestations and MPV was

significantly lower in patients with vascular activity than in patients without vascular activity [31]. This study was done on the Egyptian population as our study and to explain these contradicting results we need further large scale multicentric studies to determine the exact relationship between MPV and vascular affection in BD.

As regard the eye manifestations, Avci et al. found that MPV, PLR, and NLR values in BD patients with anterior uveitis were significantly higher than in those without anterior uveitis [53]. On the contrary was the study of Ricart et al. who reported that BD patients with posterior uveitis or thrombosis, had similar MPV levels as in patients without these manifestations [54]. Another study by Yuksel et al. found that NLR was significantly higher in relation to ocular activity in BD patients [14].

There were some limitations to our study as the small sample size and the cross-sectional nature of this study. So, further studies with larger sample size and longitudinal design including follow up of clinical as well as laboratory blood count parameters are needed to reflect the importance of these easily determined parameters on the disease activity and their role in the management of this disease with multisystem affection that are sometimes serious and potentially life threatening.

Conclusion

The blood indicis NLR, PLR, LMR and MPV are potential inflammatory markers that can be used to evaluate inflammatory status and disease activity in patients with BD. NLR and PLR showed positive relation being higher in active disease and also higher in highly active disease than in low disease activity. Also, LMR was significantly decreased in Behcet's disease patients in relation to disease activity. Furthermore, NLR, PLR levels were significantly more associated with muco-cutaneous and nervous system involvement while, LMR levels were significantly associated with muco-cutaneous, articular, gastrointestinal, and eye manifestations and MPV levels were associated with articular manifestations being significantly related to disease activity. These easily evaluated markers could help in the management of this disease with multisystem affection that are sometimes serious and potentially life threatening.

Abbreviations

ATP: Adenosine triphosphate; BD: Behcet's disease; CBC: Complete blood cell count; CRP: C-reactive protein; DMARDs: Disease modifying anti-rheumatic drugs; ESR: Erythrocyte sedimentation rate; EDTA: Ethylenediaminetetraacetic acid; hs-CRP: High-sensitivity C-reactive protein; ICBD: International Criteria for Behçet Disease; IFN-α: Interferon-alpha; IL-1β: Interleukin 1 beta; IL-6: Interleukin 6; LMR: Lymphocyte monocyte ratio; MPV: Mean platelet volume; NLR: Neutrophil lymphocyte ratio; PLR: Platelet lymphocyte ratio; SD: Standard deviation; SPSS: Statistical Package for the Social Science; TNF-α: Tumor necrosis factor-alpha; VEGF: Vascular endothelial growth factor; X^2: Chi-square test.

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Authors' contributions

Dr. DK and EI shared the conceptualization, study design, clinical work, investigations, conducting the results, and formal analysis. Prof. ZS and NM also shared conceptualization, study design, writing the paper, and formal analysis. Dr. DK was a major contributor in writing the manuscript and responsible for paper submission. All authors have read and approved the manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was assessed and approved by The Assiut University Medical Ethical Review Board (IRB no.17100568) and was conducted following the ethical principles of the Declaration of Helsinki. The study was registered at Clinical trial gov. (NCT 03747354).
Written informed consent was obtained from all participants prior to their inclusion in the study. All samples were obtained according to the guidelines approved by the Medical Ethical Committee of Assiut University.

Consent for publication

Non applicable.

Competing interests

All authors declare that they have no competing interests.

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