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Evaluation of Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio and Mean Platelet Volume in Pediatric Psoriasis Patients: A Descriptive Study

Pediatrik Psöriyazis Hastalarında Nötrofil/Lenfosit Oranı, Platelet/Lenfosit Oranı ve Ortalama Platelet Hacminin Değerlendirilmesi: Tanımlayıcı Bir Çalışma

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ABSTRACT Objective: Psoriasis is a chronic inflammatory disease and clinical symptoms start during childhood in about one third of the patients. The aim of this study is to investigate the existence of inexpensive and easily applicable laboratory parameters that can be used in the evaluation of disease activity and severity in childhood psoriasis. **Material and Methods:** This retrospective study included 72 psoriatic patients who admitted to the dermatology outpatient clinic of a tertiary university hospital within one year and 45 healthy controls under 18 years of age. Demographic and clinical data were recorded from files. Erythrocyte sedimentation rate (ESR), C-reactive protein, white blood cell (WBC), lymphocyte, neutrophil, platelet counts, mean platelet volume (MPV) value were recorded and neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio were calculated and noted. **Results:** The study included totally 117 children; 72 (45 females, 27 males) patients and 45 (23 females, 22 males) controls. In the patient group, 42 (58.3%) children had plaque type and 30 (41.7%) children had guttate type psoriasis. ESR, WBC, neutrophil counts, MPV and NLR values were significantly higher in the patient group than the control group ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p=0.002$, respectively). NLR was found to be higher in plaque type psoriatic patients compared to control group ($p=0.005$). **Conclusion:** WBC, neutrophil count, MPV and NLR values can be alternative parameters for the assesment of the disease activity in pediatric psoriasis.

Keywords: Psoriasis; pediatric psoriasis; neutrophil/lymphocyte ratio; mean platelet volume

ÖZET Amaç: Psöriyazis; kronik inflamatuar bir hastalık olup, hastaların yaklaşık 1/3'ünde klinik belirtiler çocukluk döneminde başlar. Bu çalışmanın amacı, çocukluk psöriyazisinde hastalık aktivite ve şiddetini değerlendirmede kullanılabilecek ucuz ve kolay ulaşılabilir laboratuvar parametrelerinin varlığını araştırmaktır. **Gereç ve Yöntemler:** Bu retrospektif çalışmaya, 1 yıllık süre zarfında 3. basamak bir sağlık kuruluşunun dermatoloji polikliniğine ayaktan başvuran 18 yaş altı 72 psöriyazis tanılı hasta ile 45 sağlıklı kontrol dâhil edildi. Demografik ve klinik veriler dosyalar taranarak kaydedildi. Eritrosit sedimantasyon hızı (ESH), C-reaktif protein, beyaz kan hücresi [white blood cell (WBC)], lenfosit, nötrofil, platelet sayıları, ortalama platelet hacmi [mean platelet volume (MPV)] değerleri kaydedildi ve nötrofil/lenfosit oranı [neutrophil/lymphocyte ratio (NLR)], platelet/lenfosit oranı hesaplanarak not edildi. **Bulgular:** Bu çalışmaya 117 çocuk dâhil edilmiş olup, bunların 72'si (45 kız, 27 erkek) hasta, 45'i (23 kız, 22 erkek) kontrol grubundaydı. Hasta grubunda, 42 (%58,3) çocukta plak tip, 30'unda (%41,7) guttat tip psöriyazis vardı. ESH, WBC, nötrofil sayısı, MPV ve NLR değerleri hasta grubunda kontrol grubuna kıyasla anlamlı oranda yüksekti (sırasıyla $p<0,001$, $p<0,001$, $p<0,001$, $p<0,001$, $p=0,002$). NLR, plak tip psöriyazis hastalarında kontrol grubuna kıyasla anlamlı oranda yüksekti ($p=0,005$). **Sonuç:** WBC, nötrofil sayısı, MPV ve NLR, pediatrik psöriyazisteki hastalık aktivitesini değerlendirmede kullanılabilecek alternatif parametreler olabilir.

Anahtar Kelimeler: Psöriyazis; pediatrik psöriyazis; nötrofil/lenfosit oranı; ortalama platelet hacmi

Psoriasis is a chronic inflammatory disease of the skin, nails and joints, affecting 1-2% of the population.[1] Clinical symptoms starts during childhood in about one third of the patients.[2,3] Although the most common type of psoriasis in childhood is chronic plaque type, similar to adults, the distribution, mor-

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phology, clinical symptoms and findings may vary.[1] Pediatric psoriasis can be accompanied by comorbidities such as obesity, hypertension, hyperlipidemia and diabetes mellitus as in adults.[1,2] Since recurrent attacks and possible comorbidities are associated with the disease, treatment and long-term follow-up are important.[1]

In clinical practice, for evaluating severity of the disease, accompanying systemic inflammation and response to treatment in patients with psoriasis, some parameters or scoring systems are needed. Among these; Psoriasis Area Severity Index (PASI) is one of the most commonly used parameters. However it is subjective, can be used for only plaque type psoriasis and not very easy to use during routine clinical practice. Besides; skin lesions are not the only indicator of disease activity and systemic inflammation in psoriasis, which is a systemic inflammatory disease. Considering the relationship between subclinical inflammation and possible comorbidities, it may be useful to evaluate and follow-up inflammatory parameters in psoriatic patients.[4] This has led to the idea of using some other parameters such as neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), mean platelet volume (MPV) which had been actively used as markers of inflammation in some other diseases. In literature, there are many studies investigating the relationship between the disease severity and NLR, PLR, MPV values and also utility of these parameters in determining the presence and severity of systemic inflammation in adult psoriatic patients.[5,6] Moreover in some studies it was reported that higher values of these parameters may be associated with the increased risk of cardiovascular disease.[7] Although there are many studies about the presence of systemic inflammation, its relation with the disease severity and the long-term results of the chronic inflammation in adult psoriatic patients; parameters for determining all these in children with psoriasis are rarely investigated.[8] The aim of this study is to evaluate the possible relationship between total leukocyte [white blood cell (WBC], lymphocyte, neutrophil and platelet counts, NLR, PLR, MPV values, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and type and severity of the disease, accompanying systemic subclinical inflammation.

MATERIAL AND METHODS

The study was conducted in accordance with the principles of the Declaration of Helsinki and it was approved by Tokat Gaziosmanpaşa University Faculty of Medicine Dean's Clinical Research Ethics Committee (date: October 19, 2018, no: 18-KAEK-213).

Before the study, it was predicted that there would be a moderate difference in WBC value between the patient group and the control group, and in the power analysis, it was predicted that the study could be performed with 65 patients and 41 controls with 80% power and 0.05 margin of error.

This retrospective study included 72 psoriatic patients under 18 years of age who admitted to the dermatology outpatient clinic of a tertiary university hospital within one year. During the clinical examination, patients who had a positive history for febrile illness in the last month, antibiotic use due to any illness, concomitant systemic inflammatory disease or receiving systemic immunosuppressive therapy were excluded from the study. A control group consisting of 45 children was created from patients who admitted to the pediatric outpatient clinic for routine control with similar age and gender as our psoriatic patients. Data including age, gender, age at the onset of the disease, duration and clinical type of the disease, family history of psoriasis, PASI score, nail and joint involvement, antipsoriatic drugs (topical/systemic) for the patient group and demographic characteristics of the control group were recorded. Consultation from the physical therapy and rehabilitation department was obtained for the patients who had symptoms/signs like morning stiffness lasting more than half an hour, pain/swelling in the joints or heel pain relevant for joint involvement. The complete blood count was performed using a standard automatic blood cell counter (CELL-DYN Ruby Hematology Analyzer; Abbott Laboratories, IL, USA) with ethylenediaminetetraacetic acid anticoagulated blood samples. WBC, lymphocyte, neutrophil, platelet counts, MPV value, ESR, CRP were recorded and NLR, PLR were calculated and noted.

STATISTICAL ANALYSIS

Data for continuous variables were given as mean, standard deviation or median, minimum, maximum. Data for categorical variables were given as frequency, percentage. Mann-Whitney U or Kruskal Wallis tests were used to compare non-normal distributions of variables between/among groups. Independent samples t-test or one-way ANOVA test were used to compare normal distributions of variables between/among groups. Spearman correlation coefficient was used for bivariate correlation between PASI and non-normal quantitative variables NLR, ESR and CRP. For the bivariate correlation of other variables with PASI, Pearson correlation coefficient was used. Chi-square test was used to compare the categorical data between/among groups. A p-value <0.05 was considered significant. Analyses were performed using SPSS 19 (IBM SPSS Statistics 19, SPSS inc., an IBM Co., Somers, NY).

RESULTS

There were 72 (45 females, 27 males) patients and 45 (23 females, 22 males) controls in the study. The mean age of the patient group was 12.1±3.5 (5-17 years) years and of the control group was 11.4±2.9 (6-17 years) years. The age and gender distribution of the 2 groups were similar (p>0.05).

In the patient group, 42 (58.3%) children had plaque type and 30 (41.7%) children had guttate type psoriasis. The mean age at the disease onset was 11.3±3.5 (5-17 years) years, while mean disease duration was 10.3±18 (1-100 months) months. Six (8.3%) patients had a family history of psoriasis. In 5 (6.9%) patients nail involvement was present, none of the patients had joint involvement. The mean PASI score of 42 patients with plaque type psoriasis was 6.5±2.9 (2-15). No method was used to assess disease severity in patients with guttate psoriasis. In the patient group; 3 patients were receiving systemic therapy (acitretin), the remaining patients were using topical antipsoriatic therapy (n=52) or were treatment-free (n=17) at the time of admission.

In the patient group, ESR, WBC, neutrophil count, and NLR values were significantly higher than the control group (p<0.001, p<0.001, p<0.001, p=0.002, respectively). However CRP values were similar in the groups (p>0.05). Laboratory parameters of patient and control groups are shown in Table 1.

The laboratory parameters of the plaque and guttate type psoriatic patients were compared with the control group. WBC, neutrophil count, MPV and ESR values were similar in guttate and plaque type and were significantly higher compared to control group. NLR was significantly higher in plaque type psoriatic patients compared to the control group (p=0.009). Results of this comparison are shown in Table 2.

Among the patients with plaque type psoriasis, 5 patients had moderate to severe (PASI>10) and 37 patients had mild (PASI≤10) psoriasis. In this study, there was no significant correlation or relationship between PASI score and WBC, neutrophil, lymphocyte, platelet counts, MPV, NLR, PLR values in plaque type psoriatic patients. Although there was no

TABLE 1: Laboratory parameters of the patient and control groups.

Parameters	Patients (n=72)	Control group (n=45)	p value
WBC (10^3/mL)	8.03±2.07	6.73±1.4	<0.001
Neutrophil (10^3/µL)	4.53±1.73	3.31±0.97	<0.001
Lymphocyte (10^3/µL)	2.62±0.71	2.62±0.79	0.976
Platelet (10^3/µL)	309.84±86.21	302.16±62.15	0.577
MPV (fL)	9.04±1.43	7.03±1.11	<0.001
NLR	1.54 [0.6-8.1]	1.3 [0.4-2.9]	0.002*
PLR	123.4±37.36	124.44±44.15	0.892
ESR (mm/h)	13.1±10.21	6.13±2.5	<0.001
CRP (mg/L)	2.55 [0.1-40]	3 [0.1-3.4]	0.975*

*Mann-Whitney U test was used. Indipendent sample t test was used to compare the other parameters; WBC: White blood cell; MPV: Mean platelet volume; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

TABLE 2: Comparison of the laboratory parameters of patients with disease subtypes and control group.

	Patient group (n=72)			
Parameters	**Guttate type (n=30)**	**Plaque type (n=42)**	**Control group (n=45)**	**p-value**
WBC (10^3/mL)	7.95±2.32 (a)	8.09±1.89 (a)	6.73±1.4 (b)	0.001
Neutrophil (10^3/µL)	4.51±1.85 (a)	4.55±1.66 (a)	3.31±0.97 (b)	<0.001
Lymphocyte (10^3/µL)	2.68±0.63	2.58±0.76	2.62±0.79	0.869
Platelet (10^3/µL)	321.36±79.58	301.62±90.69	302.16±62.15	0.500
MPV (fL)	8.73±1.35 (a)	9.27±1.46 (a)	7.03±1.11 (b)	<0.001
NLR	1.5 [0.85-8.1] (ab)	1.59 [0.6-5.9] (a)	1.3 [0.4-2.9] (b)	0.009*
PLR	124.28±37.05	122.78±38.03	124.44±44.15	0.979
ESR (mm/h)	11.5 [1-34] (a)	9 [1-60] (a)	5 [3-12] (b)	<0.001*
CRP (mg/L)	3 [0.1-12]	2.35 [0.1-40]	3 [0.1-3.4]	0.821*

*Kruskal Wallis test was used. One-way ANOVA was used to compare the other parameters; (abc): The same letter in lines refers to statistical insignificance; WBC: White blood cell; MPV: Mean platelet volume; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

TABLE 3: The evaluation of relation between laboratory parameters and disease activity in plaque type psoriatic patients.

Parameters	**Mild psoriasis (PASI≤10) (n=37)**	**Moderate to severe psoriasis (PASI>10) (n=5)**	**p value***
WBC (10^3/mL)	7.7 [4.7-14]	7.6 [6.1-8.2]	0.449
Neutrophil (10^3/µL)	4.4 [1.9-9]	3.6 [3.2-4.43]	0.200
Lymphocyte (10^3/µL)	2.5 [1-4.2]	2.8 [1.9-3.9]	0.268
Trombocyte (10^3/µL)	291.6 [89-493]	266 [260-350]	0.923
MPV (fL)	9.8 [5-12.1]	8.5 [6.9-10.8]	0.275
NLR	1.6 [0.6-5]	1.28 [0.8-1.68]	0.139
PLR	123.3 [59.6-210]	95 [66.6-148.9]	0.168
ESR (mm/h)	9 [1-46]	16 [1.8-60]	0.756
CRP (mg/L)	2.2 [0.1-40]	3.4 [0.5-3.4]	0.770

*Mann-Whitney U test was used; PASI: Psoriasis Area and Severity Index; WBC: White blood cell; MPV: Mean platelet volume; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.

significant releationship and correlation between inflammatory parameters and disease severity in this study, we think that data can be interpreted more effectively by increasing the number of patients with severe disease. Mean values of the parameters and results of comparison are shown in Table 3.

DISCUSSION

In this study we found that, WBC, neutrophil count, MPV, NLR and ESR values were significantly higher in the pediatric psoriatic patients than the controls and, NLR was significantly higher in plaque type psoriatic patients compared to the control group.

Psoriasis is a chronic inflammatory disease and it is well documented that subclinical systemic inflammation may persist in psoriasis in spite of regression of skin lesions and this inflammation is linked to high risk for cardiovascular diseases especially atherosclerosis.[9] So objective, easy to use and inexpensive parameters are needed to evaluate this ongoing subclinical systemic inflammation.[9] Recently, high-sensitivity CRP has been reported as an inexpensive and useful biomarker that can be used in the detection of subclinical atherosclerosis.[10] There are some studies about the use of NLR and PLR values in the follow-up of subclinical inflammation in adult plaque type psoriasis and the relationship with the clinical severity of the disease and comorbidities.[5,11] Significant relation was established between NLR, PLR values and disease severity, disease duration or arthritic involvement and cardiometabolic co-

morbidities in adult psoriatic patients in several studies.[6,11-13] There are also studies reporting no relationship between these parameters and disease severity in the adult population.[14] However these parameters are very rarely investigated in pediatric psoriasis.[8] The NLR and PLR values are considered as parameters that are relatively more stable and can be used in the follow-up of inflammation compared to other hemogram parameters such as WBC count which can easily change by dehydration/overhydration.[5] In our study, WBC, neutrophil counts and NLR values were found to be higher in the patient group than the control group. The fact that inflammatory parameters were found to be similarly high in both guttate and plaque type psoriasis suggested that the inflammatory process caused by psoriasis may play a more dominant role compared to the inflammatory process secondary to the infectious agent, which is often the trigger in guttate psoriasis. There was no significant difference in platelet, lymphocyte counts and PLR value between patient and control groups.[13,15,16]

In the current study, MPV was significantly higher in the patient group. It is known that activation of platelets plays an important role in inflammation and degree of the platelet activity is related to their volume.[17]

Decreased MPV value is common in the pediatric ages due to acute inflammation caused by common infections.[18] Increased MPV value together with normal platelet count is observed in many chronic diseases such as cardiovascular disease, diabetes mellitus, cerebrovascular disease and malignancies.[12] However, in literature, there are different and conflicting results regarding MPV in psoriatic patients. In some studies MPV was found related with the disease severity or activity whereas no relation was established in some other studies.[12,15] In 2022 a meta-analysis including 13 studies with 1,331 psoriasis patients and 919 controls, was published about the usability of MPV and red cell distribution width (RDW) in the early diagnosis and evaluation of the severity of the psoriasis. There was significant relation between the presence of the disease and MPV and RDW however no significant relation was found between the MPV and disease severity.[19] In another meta-analysis about platelet-associated parameters in psoriasis; 22 studies with 1,749 patients and 1,538 controls were included. It was found that PLR, MPV and platelet distribution width were significantly higher in the patient group compared to the control group, which may indicate low-grade systemic inflammation and platelet activation in patients with psoriasis.[20]

In some studies, NLR, PLR and MPV were found related or correlated with the disease severity or activity in adult psoriasis.[11-13,21] In our study, there was no significant correlation or relationship between PASI score and laboratory parameters in plaque type pediatric psoriatic patients. This suggested that although systemic inflammation markers increase during the course of the disease, they may not be associated with PASI which is a clinical index of skin involvement.[9]

Parameters for determining the disease activity are also considered for the evaluation of response to treatment during follow-up of patients. In the study of Asahina et al., it was also mentioned that there was a significant decrease in NLR and PLR values after treatment with biological agents. In another study conducted by Erek Toprak et al., after the application of narrow band ultraviolet B treatment in psoriatic patients, significant decrease in NLR values was not observed.[22,23] This was thought to be due to the residual subclinical inflammation in that patient group. We think that further studies are required for documenting the utility of these parameters in the evaluation of response to treatment in disease subtypes in both pediatric and adult psoriatic patients.

To the best of our knowledge, our study is the first to investigate laboratory parameters that are inexpensive and easy to use in assessing the disease activity in pediatric psoriatic patients. However for more accurate results, larger series and multicenter studies are needed.

STUDY LIMITATIONS

There are some limitations in this study. First of all, the study was designed as a single center and retrospective study with a relatively small number of patients. Due to its retrospective nature, we were unable to know exactly the hydration status of the patients or blood sampling method that can change the stud-

ied markers. In addition, in order to exclude the presence of infection that could trigger psoriasis attack in the patient group, the history of infection or antibiotic use in the preceding month was questioned but no laboratory examination, such as blood or throat culture was performed. Prospective studies with larger series are needed.

CONCLUSION

WBC, neutrophil count, MPV, NLR and ESR values can be alternative parameters for the assesment of the disease activity in pediatric psoriasis. Apart from PASI, which is a clinical indicator of skin involvement, it may be useful to monitor inflammatory parameters that may indicate subclinical inflammation and possible comorbidity risks of pediatric psoriatic patients. Multicenter, prospective studies with larger series are required in pediatric patients with psoriasis to investigate the utility of the parameters such as NLR, MPV which are considered to be markers of subclinical systemic inflammation.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Atiye Akbayrak, Tuba Kasap;* ***Design:*** *Atiye Akbayrak, Tuba Kasap;* ***Control/Supervision:*** *Atiye Akbayrak, Tuba Kasap;* ***Data Collection and/or Processing:*** *Atiye Akbayrak, Tuba Kasap, Zennure Takçı, Havva Yıldız Seçkin, Ali Gül, Ergün Sönmezgöz;* ***Analysis and/or Interpretation:*** *Atiye Akbayrak, Tuba Kasap, Osman Demir;* ***Literature Review:*** *Atiye Akbayrak, Tuba Kasap;* ***Writing the Article:*** *Atiye Akbayrak, Tuba Kasap;* ***Critical Review:*** *Atiye Akbayrak, Tuba Kasap.*

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