Original Article

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Evaluation of Hematological Parameters in Children with Idiopathic Facial Paralysis: A Case-control Study

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Abstract

Aim: Idiopathic peripheral facial paralysis [Bell's palsy (BP)] is the most common cause of acute, one-sided facial paralysis, whose etiopathogenesis is currently unknown. However, inflammation is considered to play a role in etiopathogenesis. In this study, we examined the relationship between hematologic parameters and indices in children with BP.

Methods: The study included 60 pediatric patients diagnosed with BP between December 2017 and May 2022 and 60 healthy controls of the same age and gender. The relationship between the patient and control cohorts and between the severity of the disease and inflammation markers was analyzed. Low-severe BP (House-Brackmann classification grade 2-3) and high-severe BP (House-Brackmann classification grade 4-5) were grouped. Complete blood count parameters and hematologic indices [neutrophil count/lymphocyte count (NLR), platelet count/lymphocyte count (PLR), monocyte count/lymphoid count (MLR), and platelet mass index] were recorded as inflammation markers.

Results: 55% of the patients had BP on the right side, 48.3% had grade 3, and 30.0% had grade 4 facial paralysis. Leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts were significantly higher in the patient group than in the control group (p-values p<0.001, p=0.006, p=0.027, p=0.009, respectively). The low-severe BP group had significantly higher leukocyte counts than the high-severe BP group. However, there was no significant difference between the other hematologic parameters and indices (NLR, PLR, MLR, and platelet mass index).

Conclusion: Children with BP had higher counts of leukocytes, neutrophils, lymphocytes, monocytes, and platelets than children in the control group. Thus, we believe that these parameters can be used in the diagnosis, differential diagnosis, and treatment of patients with BP.

Keywords: Child, platelet count, facial paralysis, diagnosis-differential, blood cell count

Introduction

Idiopathic peripheral facial paralysis [Bell's palsy (BP)] is a sudden onset, usually partial or total muscular paralysis on either side of the face. It is the most common motor cranial neuropathy that can occur as a result of damage at any level along the anatomical course of the facial nerve from the motor nucleus in the brain stem until it reaches the facial mimic muscles (1). The incidence is 19-21 per 100,000 children younger than 18 years old. Patients usually present with a sudden onset of unilateral facial paralysis that lasts from a few hours to a day. Mild pain radiating behind the ear, numbness of the face, increased

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sensitivity to sound, and taste disturbances are other accompanying symptoms. Although the etiopathogenesis has not been fully elucidated, inflammation is considered to play a role (2). In the literature, prognostic factors for peripheral facial paralysis include age, severity of the disease, period between the onset of symptoms and treatment, electrophysiological changes, and history of recurrence (2-4). In adults, corticosteroids offer important benefits, particularly when they are administered early during the disease, whereas there are no standardized treatment guidelines for children. Peripheral facial paralysis in children generally has a good prognosis, but if it does not fully regress, it can affect quality of life in the long term, causing problems with drinking, eating, and speaking and even affecting social life (2). Magnetic resonance imaging (MRI) of patients with BP shows inflammation of the facial nerve (5).

Further evidence supporting an inflammatory etiology is the high neutrophil count/lymphocyte count (NLR) found in patients with BP (5-8). In another study, the relationship between BP and inflammatory markers such as white blood cells (WBCs), neutrophils, lymphocytes, monocytes, platelet count/lymphocyte count (PLR), NLR, mean platelet volume (MPV), and red blood cell distribution width (RDW) was evaluated, and a statistically significant difference was found between lymphocytes, NLR, and PLR between the patient and control groups (9). Although there are many studies in the literature evaluating hematologic parameters and indices as diagnostic and prognostic markers in adult patients with BP, there are not enough studies in pediatric patients.

We hypothesized that there may be a strong relationship between disease severity and hematological parameters or indices indicating inflammation in BP patients. Therefore, we aimed to analyze the relationship between pediatric patients with BP and healthy controls and between disease severity and hematologic parameters and hematologic formulas [e.g., hemoglobin (Hb), mean corpuscular volume (MCV), RDW, MPV, platelet distribution width (PDW), leukocyte, neutrophil, lymphocyte, and platelet count] to investigate the relationship between NLR, PLR, MLR (monocyte count/lymphoid count), and platelet mass index and to evaluate the prognostic utility of these parameters.

Methods

Compliance with Ethical Standards

The study was conducted in accordance with the principles of the Helsinki Declaration and was endorsed by the Afyonkarahisar Health Sciences University, Non-Conventional Clinical Research Ethics Committee (approval no.: 2022/12, date: October 7, 2022). Informed consent was obtained.

Study Design

Our study enrolled 60 pediatric patients with idiopathic peripheral facial paralysis who were admitted to the Pediatric Neurology Outpatient Clinic of Afyonkarahisar Health Sciences University Faculty of Medicine Hospital with acute unilateral facial weakness between December 1, 2017 and May 31, 2022. Sociodemographic characteristics, detailed ear-nose-throat examination, neurologic and systemic examination findings, laboratory tests (complete blood count and biochemistry analysis), audiologic evaluation and MRI results, and treatment received by all patients at the time of diagnosis were reviewed from the electronic outpatient clinic records.

Patient Selection

Children with a diagnosis of congenital facial paralysis (2 patients), otitis media (2 patients), Ramsay-Hunt syndrome (1 patient), history of trauma before paralysis (2 patients), history of systemic inflammatory diseases such as diabetes (1 patient), and additional abnormal neurological findings on neurological examination were excluded. In addition, children with underlying chronic diseases such as malignancy (1 patient) and those taking medication for these diseases were excluded. Cranial MRI was performed in every child with acute facial weakness, and tumor-related facial paralysis was excluded. Sixty pediatric patients with idiopathic BP were enrolled in our study. The control group included 60 healthy children who were admitted to the pediatric outpatient clinic for routine healthy child follow-up and had no history of any infection in the last 15 days and no chronic disease (Figure 1). The patients were evaluated by an otorhinolaryngologist according to the House-Brackmann classification of facial paralysis. According to this classification, grade 1 is classified as normal and symmetrical function in all areas, grade 2 as mild dysfunction, grade 3 as moderate dysfunction, grade 4 as moderate to severe dysfunction, grade 5 as severe dysfunction, and grade 6 as total paralysis (10,11). Paralysis staging was performed based on this classification at the time of initial admission and 1 month after treatment. Patients are considered to have responded to treatment if there is a decrease in staging in the first month after treatment compared with the staging at the time of initial admission. All patients diagnosed with BP routinely receive standard treatment in our clinic if there are no contraindications. According to Hb scoring, 1 mg/kg/day prednisolone is started in patients with grades 1-2 according to Hb scoring and discontinued by tapering in 15 days, and 2 mg/kg/day prednisolone (maximum dose 60 mg/day) is started in patients with grades 3-5 in the first week and discontinued by tapering in 15 days. No pediatric patient received antiviral treatment (12,13). The patient and control groups were not tested for coronavirus

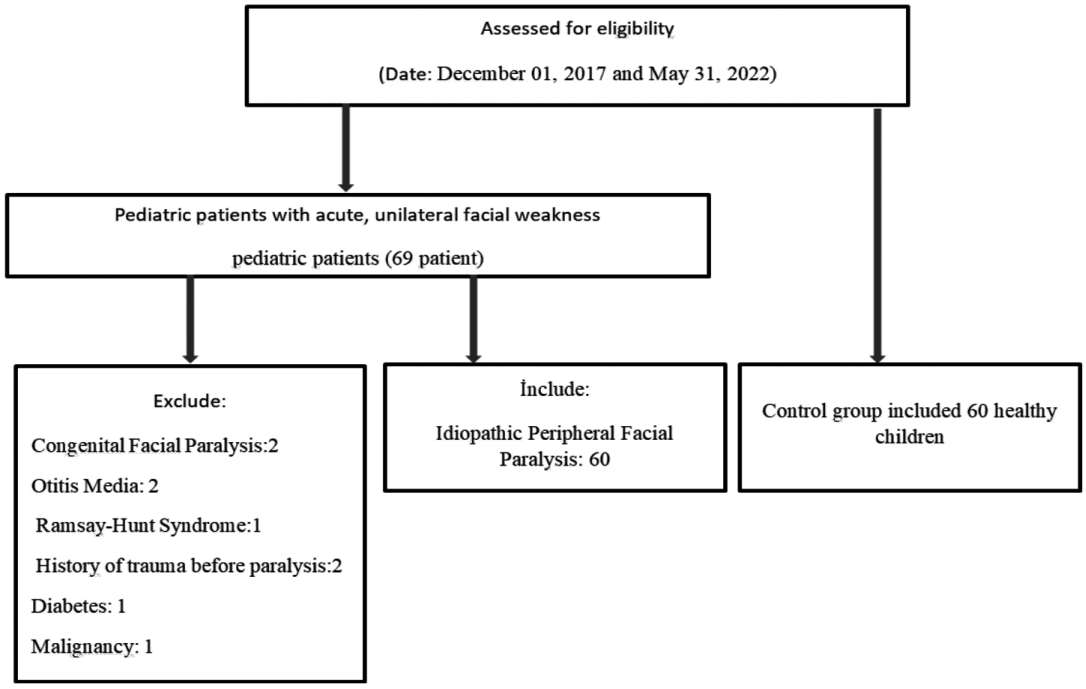

Figure 1. Patients' selection diagram

disease-2019 (COVID-19) because they did not have complaints such as fever and cough related to COVID-19.

Hematological Testing and Evaluation

The complete blood counts and C-reactive protein (CRP) values of the patients were taken before steroid treatment. Hb, MCV, RDW, MPV, PDW, leukocyte, neutrophil, lymphocyte, platelet count, and CRP were recorded from laboratory tests of the patient and control groups. Calculated leukocyte formulas include NLR, PLR, MLR, and platelet mass index (platelet count times MPV). Low-severe BP: Group 1 (House-Brackmann classification grade 2-3), and high-severe BP: Group 2 (House-Brackmann classification grade 4-5) were grouped. The relationship between hematologic parameters and indices between the patient and control cohorts was investigated.

Statistical Analysis

All statistical analyses were performed using the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows, Version 18.0, Chicago). Descriptive statistics are presented as percentage frequency for categorical data, mean and standard deviation (mean ± standard deviation) when continuous data conform to a normal distribution, and median and quartiles [median quartile 25-75)] when not conforming to a normal distribution. The conformity of continuous data to a normal distribution was evaluated using the Kolmogorov-Smirnov test. For continuous data that fit the normal distribution, a Student's t-test was used to compare paired groups, and a one-way analysis of variance (ANOVA) was used to compare ternary groups. In cases of statistically significant differences found as a result of ANOVA, Tukey's Honestly Significant Difference test was used for intragroup comparisons. The Mann-Whitney U test was used to compare paired groups, and the Kruskal-Wallis H test was used to compare ternary groups. In cases of a statistically significant difference because of the Kruskal-Wallis H test, the Mann-Whitney U test with Bonferroni correction was used for intragroup comparisons. The chi-square test was used to compare the distributions of categorical data. A p-value of 0.05 was accepted as statistically significant.

Results

The study included 60 pediatric patients with idiopatic facial paralysis and 60 healthy controls of the same age and gender. The sociodemographic and clinical characteristics of the patient group are summarized in Table 1. The mean age of the patient group was 10.35±3.91 years, and 56.7% were girls. 55% of the patients had BP on the right, 48.3% had grade 3, and 30.0% had grade 4 facial paralysis (Table 1). 56.7% of the patient group (n=34) and 48.3% of the control group (n=29) were female, and there was no statistically significant difference between their gender distributions (p=0.361). The mean age of

the patient group was 10.35±3.91 years and that of the control group was 10.20±3.64 years, and there was no statistically significant difference (p=0.826) (Table 2).

There were no statistically significant differences in Hb, MCV, and RDW values between the patients and controls. The median leukocyte count was 8,270/mm^3 (7,300-10,567) in the patient group and was statistically significantly higher than that in the control group (p<0.001). The median values of neutrophil, lymphocyte, monocyte, and platelet counts were significantly higher in the patient group than in the control group, and there was a statistically significant difference between the patient and control groups (p-values were p<0.001, p=0.006, p=0.027, p=0.009, respectively). There were no statistically significant differences among the MPV, NLR, PLR, MLR, CRP, and platelet mass indexes of patients and controls (Table 2).

When comparing the patient groups with the House-Brackmann classification., those with grades 2 and 3 were classified as having low-severe BP, and those with grades 4 and 5 were classified as having high-severe BP. No statistically significant difference was observed between the age, Hb, MCV, RDW, MPV, NLR, PLR, MLR, CRP, and platelet mass index values of the groups (Table 3). When leukocyte counts were compared between the control group and the low-severe BP, low-severe BP, and high-severe BP groups, leukocyte counts were higher in both patient groups than in the control group (p<0.001). A statistically significant difference was found between the neutrophil, lymphocyte, monocyte, and platelet counts between the control group and the low-severe BP group, with p-values of p=0.001, p=0.009, p=0.006,

Table 1. Sociodemographic and Bell's palsy-related characteristics of patients with facial paralysis

Demographics	n (%)
Age (years)	10.35±3.91
Gender	
Female	34 (56.7%)
Male	26 (43.3%)
Laterality (side)	
Right	33 (55%)
Left	27 (45%)
Grade	
Grade 2	9 (15%)
Grade 3	29 (48.3%)
Grade 4	18 (30.0%)
Grade 5	4 (6.7%)

Table 2. Patient and control group demographics, clinical and laboratory characteristics

Characteristic	Patient group	Control group	p-value
Age (years)	10.35±3.91	10.20±3.64	0.826[a]
Gender			
Female	34 (56.7%)	29 (48.3%)	0.361[b]
Male	26 (43.3%)	31 (51.7%)	
Hb (g/dL)	13.44±1.49	13.65±1.10	0.398[a]
MCV (fL)	81.70±5.83	83.31±4.02	0.082[a]
RDW (%)	13.20 (12.43-13.78)	13.00 (12.40-13.58)	0.229[c]
Leukocyte count (/mm^3)	8270.00 (7300-10567)	6840.00 (5615.00-7695.00)	**<0.001[c]**
Neutrophil count (/mm^3)	4335.00 (3002.50-6205.00)	3110.00 (2672.50-4115.00)	**<0.001[c]**
Lymphocyte count (/mm^3)	3010.00 (2322.50-3577.50)	2635.00 (2070.00-2875.00)	**0.006[c]**
Monocyte count (/mm^3)	575.00 (460.00-720.00)	505.00 (445.00-577.50)	**0.027[c]**
Platelets (/mm^3)	335500.00±86437.10	295233.33±80724.76	**0.009[a]**
MPV (fL)	9.68±0.95	9.99±0.89	0.071[a]
NLR	1.42 (0.98-2.29)	1.32 (0.96-1.62)	0.173[b]
PLR	120.27-47.94	117.02-35.59	0.674[b]
MLR	0.19 (0.14-0.25)	0.20 (0.16-0.25)	0.553[b]
CRP (mg/dL)	0.10 (0.02-0.30)	0.10 (0.10-0.10)	0.601[b]
Platelet mass (MPV X PLT count/1000)	3151.20 (2694.45-3623.53)	2929.45 (2347.65-3422.55)	0.069[b]

[a]: Student's t-test
[b]: Chi-square test
[c]: Mann-Whitney U test
Hb: Hemoglobin, MCV: Mean corpuscular volume, RDW: Red blood cell distribution width, MPV: Mean platelet volume, NLR: Neutrophil count/lymphocyte count, PLR: Platelet count/lymphocyte count, MLR: Monocyte count/lymphoid count, PLT: Platelet, CRP: C-reactive protein

Table 3. Relationship between disease severity and hematologic indices and parameters (3 groups)				
Characteristic	**Control**	**Group 1**	**Group 2**	**p-value**
Age	10.20-3.64	10.65-3.69	9.82-4.28	0.699[a]
Numbers	60	38	22	
Hb (g/dL)	13.65-1.10	13.52-1.38	13.32-1.70	0.599[a]
RDW (%)	13.00 (12.40-13.58)	13.20 (12.55-13.60)	13.05 (12.30-13.80)	
Leukocyte count (/mm³)	6788-1313	9782-3709	7973-1801	**<0.001[&*a]**
Neutrophil count (/mm³)	3110.00 (2672-4115)	4610 (3047-6895)	4005 (2725-5327)	**0.001[&b]**
Lymphocyte count (/mm³)	2635 (2070-2875)	3055 (2522-3637)	2855 (2002-3452)	**0.009[&b]**
Monocyte count (/mm³)	505 (445-577)	640 (482-742)	485 (412-652)	**0.006[&b]**
Platelets (/mm³)	295233-80724	334947-76385	336454-103484	**0.035[&b]**
MPV (fL)	9.99-0.89	9.76-0.97	9.55-0.91	0.141[a]
NLR	1.32 (0.96-1.62)	1.47 (0.98-2.34)	1.33 (0.97-2.33)	0.366[b]
PLR	117.02-35.59	113.49-44.05	131.99-53.03	0.239[a]
MLR	0.20 (0.16-0.25)	0.19 (0.14-0.25)	0.17 (0.14-0.25)	0.76[b]
CRP (mg/dL)	0.10 (0.10-0.10)	0.10 (0.02-0.29)	0.12 (0.03-0.35)	0.733[b]
Platelet mass index	2939763.33-830573.94	3250500.00-745623.78	3148790.91-765966.82	0.155[a]

[&]: Between the control group and Group 1
[*]: Between Group 1 and Group 2
[a]: One-way analysis of variance (ANOVA)
[b]: Kruskal-Wallis H test
Hb: Hemoglobin, RDW: Red blood cell distribution width, MPV: Mean platelet volume, NLR: Neutrophil count/lymphocyte count, PLR: Platelet count/lymphocyte count, MLR: Monocyte count/lymphoid count, platelet mass index (platelet count x MPV), CRP: C-reactive protein

and p=0.035, respectively. Recurrence of the disease was observed in 5 of our patients with BP; however, there was no significant association between the group of recurrent patients and disease severity.

Discussion

Because the facial nerve has a long intracranial journey and the facial canal is anatomically close to the temporal bone, it can be easily affected by inflammation caused by diseases such as infection, trauma, and tumors (12,14,15). Although the etiopathogenesis is not yet fully understood, it has been suggested that viral, inflammatory, and immune-mediated inflammation play a major role in the etiopathogenesis of BP (15,16). Leukocytes, neutrophils, and monocytes play an active role in the proinflammatory and anti-inflammatory processes at the site of inflammation and are also essential in the initiation and maintenance of the immune response against foreign proteins (17,18). Platelets are cells generated by megakaryocytes of the bone marrow and have an active role in inflammation by producing and releasing various cytokines that affect the inflammation mechanism, similar to neutrophils and macrophages, as well as controlling bleeding (19). In our study, we demonstrated that leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts were higher in children with BP than in the control group and that an inflammatory process occurred in these patients. It has been reported that the function of platelets can be evaluated more accurately with platelet mass index than platelet count or platelet volume (20). We didn't find a significant link between BP patients and the control group or between low-severity BP patients and high-severity BP patients in our study. However, we did find that the number of platelets was higher in BP patients than in the control group. This makes us think that the platelet mass index will be higher in BP patients when it comes to inflammation in studies with more cases. Our study is the first to evaluate the platelet mass index in children with BP.

It has been demonstrated that parameters such as NLR, PLR, and MLR, which can be easily calculated from complete blood count parameters, are associated with disease severity and prognosis in inflammatory diseases (21). There are many studies showing that NLR is significantly higher in patients with BP than in the control group (1,5,9,14). Neutrophil count/lymphocyte count has also been shown to play a role in disease prognosis (8,9,14). Cayir and Kilicaslan (14) reported that NLR was higher in the non-recovery group, and WBC count and PLR were similar between the recovery and non-recovery groups. Similarly, the NRL was significantly higher in the non-recovery group, but there were no significant differences in PLRs between the recovery and non-recovery groups (22). In a recent study comparing 88 BP patients with 50 healthy control groups, it was shown that there was a statistically significant increase in systemic inflammatory index, neutrophil, and NLR levels

in the BP group and that they are useful parameters in showing the prognosis of the disease (16). Ayşel et al. (23) also reported that NLR was associated with disease severity (higher in grades 4-6) and prognosis in pediatric BP patients. Similar to our study, they did not detect any difference between MPV and PLR in relation to disease severity. Ulusoy et al. (24) found no correlation between NLR and PLR and the prognosis of the disease. In this study, we found no relationship among parameters such as NLR, PLR, MLR, and the severity of the disease between the BP and control groups or between mild and severe severity of the disease in patients with BP. Similar to our study, Atan et al. (6) also found no association between NLR, PLR, or disease severity. Although we detected significant differences in terms of leukocyte, neutrophil, lymphocyte, and monocyte numbers between the patient and control groups, we could not detect any difference in PLR, NLR, or MLR values between the patient and control groups or between the mild and severe disease groups. We attribute this to the small number of patients. Karatoprak and Yilmaz (25) followed 102 children with BP and reported that 101 children showed complete recovery and that there was no relationship between NLR and RDW and early recovery. In our study, complete recovery was observed in all children. In approximately 1-2 years of follow-up, five patients developed facial paralysis again and were re-treated. It was observed that the patients recovered completely in the follow-up, and no recurrence was observed.

Study Limitations

The limitations are the small number of patients due to the single-center design and, in particular, the small number of grade 4-5 patients. Despite these limitations, the selection of a control group of similar age and gender to the patient group in our study provides safe results in terms of hematological parameters. In addition, this study makes a significant contribution to the literature in terms of evaluating several hematological parameters in children.

Conclusion

Increased leukocyte, neutrophil, lymphocyte, monocyte, and platelet counts in children with BP compared with those in the control group support the inflammatory process considered responsible for the etiopathogenesis of this disease. Thus, we suggest that these parameters can be used in the diagnosis, differential diagnosis, and treatment of patients with BP. We would like to emphasize that we could not detect a significant correlation between the severity of the disease and hematologic parameters and indices because of the small sample size of our study and that large-scale studies are warranted in this regard.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the principles of the Helsinki Declaration and was endorsed by the Afyonkarahisar Health Sciences University, Non-Conventional Clinical Research Ethics Committee (approval no.: 2022/12, date: October 7, 2022).

Informed Consent: Informed consent was obtained.

Authorship Contributions

Surgical and Medical Practices: H.S.S., S.K., D.C., Concept: H.S.S., N.E., D.C., Design: H.S.S., Y.D.K., D.C., Data Collection or Processing: H.S.S., S.K., Y.S., D.C., Analysis or Interpretation: H.S.S., N.E., Y.S., D.C., Literature Search: H.S.S., Y.D.K., D.C., Writing: H.S.S., Y.D.K., D.C.

Conflict of Interest: No conflict of interest was declared by the authors.

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