

ORIGINAL RESEARCH

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The value of blood parameters as a diagnostic biomarker for congenital sensorineural hearing loss

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Abstract

Blood parameters such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) have been used as systemic inflammation and infection indicators, recently. In this study, we aimed to determine the diagnostic value of blood parameters such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) for congenital sensorineural hearing loss (CSNHL) and to investigate its relationship with disease severity. Fifty-three pediatric patients (29 males, 24 females; mean age 23.85 ± 5.35 months; distribution 12-35 months) diagnosed with CSNHL and 53 healthy individuals (32 males, 21 females; mean age 22.92 ± 6.10 months; distribution 12-35 months), were included in this retrospective study. NLR, PLR and MPV values of CSNHL and control groups were calculated and compared statistically. The correlation between blood count values and hearing loss degree was investigated in CSNHL group. NLR levels were significantly higher in the CSNHL group than in the control group. (Mean NLR: CSNHL group = 2.71 ± 1.11 ; Control group = 2.28 ± 0.99 ; $p = 0.04$). PLR levels were also significantly higher in the CSNHL group compared to the control group. (Mean PLR: CSNHL group = 139.19 ± 59.41 ; Control group = 111.89 ± 59.91 ; $p = 0.02$). There was no correlation between NLR and PLR values and hearing values. NLR and PLR values obtained by low-cost tests, which can be applied easily on patients with CSNHL, can be used as a new inflammatory biomarker. Further studies with larger patient series are needed to confirm these findings.

Keywords: Congenital sensorineural hearing loss, neutrophil, platelet, lymphocyte, ratio

Introduction

Pediatric congenital sensorineural hearing loss (CSNHL) affects 1.1% to 19.5% of children and disrupts language development, psychosocial maturation, and social adjustment of the patients, leading to individual and social problems [1-4]. Hearing loss can be classified as syndromic (20%-30%) and non-syndromic (70%-80%). In pediatric hearing loss; although genetic mutations and factors such as environmental factors (exposure to noise and tobacco smoke, heavy metal toxicity, cisplatin, gentamicin) and infectious factors (cmv, measles, mumps, meningitis) have been implicated, most of the cases remain idiopathic [1-4].

Neutrophils and lymphocytes play important roles in inflammatory and immunological processes. Under inflammatory conditions, neutrophil and lymphocyte numbers undergo transient changes. The increase in neutrophil count (neutrophilia) and decrease in lymphocyte count (lymphopenia) reflect any inflammatory condition in the human body [5-9]. Mean platelet volume (MPV) may also be used as an indicator of inflammation [10-12].

Ear-nose-throat diseases such as idiopathic sudden sensorineural hearing loss (ISSNHL) [5,6], tinnitus [7], Bell palsy [8] and vestibular neuritis [9] are associated with NLR and PLR. In addition; these parameters are suggested to reflect an inflammatory response and disease activity in many inflammatory and autoimmune diseases such as chronic otitis media (COM) with effusion [13], Familial Mediterranean Fever(FMF) [14], Systemic Lupus Erythematosus (SLE) [15] and coronary artery diseases such as cardiovascular diseases [16,17]. Furthermore, these parameters have also been suggested to be high in some malignant diseases and indicate poor prognosis [18-21]. In our previous study, we had demonstrated that pediatric patients with CSNHL were exposed to oxidative stress [1]. Inflammation may occur as a result of OS. Chronic inflammation may play a critical role in the development and progression of the physiopathogenesis of CSNHL. We assume that blood parameters such as NLR, PLR and MPV can be used as systemic inflammation indicators in patients with CSNHL.

In this study, by accepting that chronic inflammation forms the basis of the formation process of CSNHL, we evaluated NLR, PLR, and MPV levels, which are the parameters of systemic inflammation in these patients. Also, we aimed to investigate the correlation of the levels of these parameters with the severity of hearing loss.

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Materials and Methods

Fifty-three pediatric cases diagnosed with bilateral profound congenital SNHL and followed-up in the cochlear implant program between August 2015 and February 2019 at Harran University, School of Medicine, Department of Otorhinolaryngology, were included in this retrospective case-control study as a patient group. The control group included patients who were admitted to our center for hearing screening, and their hearing was within normal limits. The control group consisted of 53 healthy individuals with age and sex-matched with that of the patient group. The files of the cases included in the study were analyzed retrospectively through a systematic database search. The study protocol was approved by the Ethics Committee of Harran University, School of Medicine (13.06.2019 / 06-38), and was conducted under the ethical principles described by the Helsinki Declaration. A detailed history was obtained from the parents of the patient group, and the healthy control group and basic otoscopic examinations were performed. Pure tone/free field audiometry, tympanometry, acoustic reflex measurements, auditory brainstem response (ABR) and auto acoustic emission (OAE) tests of all cases were evaluated.

Exclusion Criteria

Patients with congenital inner ear anomalies, syndromic patients, inflammatory or infectious diseases, autoimmune diseases, history of temporal bone trauma, history of neuro-otologic surgery, liver, renal, hematologic, cardiovascular, metabolic and neurological diseases and malignancies and white cell count $<4 \times 10^3$ and $>11 \times 10^3$, were excluded from the study.

Laboratory Methods

Blood samples were collected from the peripheral veins of all participants using the Cell-Dyne Ruby fully automated hemogram device through the optical laser scattering method (Abbott Cell-Dyne Ruby; IL 60064, Chicago, USA). CBC parameters, white blood cell (WBC), hemoglobin, erythrocytes, leukocytes, neutrophils, lymphocytes, platelet counts, and MPV of all participants were analyzed with an automated hematology analyzer. The NLR value was calculated by dividing neutrophil count by lymphocyte count, and PLR value was calculated by dividing platelet count by lymphocyte count.

Leukocyte, neutrophil, lymphocyte, platelet, NLR, PLR, and MPV values of both groups were separately compared statistically. NLR, PLR and MPV values found to have statistically significant differences between the two groups were correlated with the results of ABR test

Statistical Analysis

Statistical analyses were performed using SPSS 25.0 (IBM Corporation, Armonk, NY, USA). Parametric tests were used for normally distributed data, and non-parametric tests were used for non-normally distributed data in the comparison of blood parameters of the patient group and control group. $P < 0.05$ value was considered to be significant.

Results

Demographic characteristics and all laboratory findings of the participants are shown in Table 1. 53 individuals (male: 29 (54.7%); female: 24 (45.2%)) were included in the CSNHL group and 53 individuals (male: 32 (60.3%); female: 21 (39.6%)) were

included in the control group. The mean age was 23.85 ± 5.35 months (distribution 11 to 33 months) in the CSNHL group and 22.92 ± 6.10 months (distribution 12 to 35 months) in the control group. When the groups were compared in terms of gender and age distribution, no statistically significant difference was found, and these two groups were interpreted as statistically comparable ($p > 0.05$). According to the mean values of ABR measurements, the patient group was recorded to have bilateral severe and profound SNHL (Right ear: 101.57 ± 19.24 dBnHL; Left ear: 98.48 ± 13.41 dB nHL). According to the mean values of ABR measurements, the hearing levels were normal in the control group (Right ear: 15.03 ± 5.46 dBnHL; Left ear: 14.4 ± 3.22 dB nHL). (Table 1)

Table 1. The demographic characteristics and laboratory values of the csnhl patients and control groups

		Patients group (n=53)	Control group (n=53)	P value
Age (months)		23.85 ± 5.35	22.92 ± 6.10	0.409
Gender (male/female)		29/24	32/21	
ABR (dB nHL)	Right	101.57 ± 19.24	15.03 ± 5.46	0.001
	Left	98.48 ± 13.41	14.43 ± 3.22	0.001
WBC		7.740 ± 1.550	7.533 ± 1.274	0.454
Neutrophil, ×10 ³ /L s,		6.777 ± 1.483	5.294 ± 0.928	0.001
Lymphocytes, ×10 ³ /L		2.691 ± 0.685	2.618 ± 0.804	0,618
PLT, ×10 ³ /L		310.35849±82.81479	279.02641±76.12790	0.045
MPV, fL		9.243 ± 4.236	9.035 ± 4.283	0.802
NLR		2.714 ± 1.110	2.287 ± 0.996	0.04
PLR		139.195 ± 59.418	111.899 ± 59.911	0.02

Data are presented as means $\pm$ standard deviation. ABR: auditory brainstem response. dB nHL; decibel normalized hearing level. WBC: white blood cell. NLR: neutrophil to lymphocyte ratio. PLR: platelet to lymphocyte ratio. MPV: mean platelet volume. PLT: platelet

Table 2. Correlation between ABR values of patients group and NLR and PLR values

		NLR	PLR	NEUTR	PLT
ABR	Pearson Correlation	0.254	0.226	0,072	-0,112
	p	0.066	0.104	0,61	0,425
	N	53	53	53	53

p value is calculated by 2-tailed t-test. ABR: auditory brainstem response. NLR: neutrophil to lymphocyte ratio. PLR: platelet to lymphocyte ratio. NEUTR: neutrophil. PLT: platelet.

The mean NLR value was 2.71 ± 1.11 in the patient group and 2.28 ± 0.99 in the control group. NLR value was found to be significantly higher statistically in the patient group ($p = 0.04$). The mean PLR value was 139.19 ± 59.41 in the patient group, whereas it was 111.89 ± 59.91 in the control group. PLR value was found to be significantly higher statistically in the patient group ($p = 0.02$).

As shown in Table 2, there was no significant correlation between ABR test results and laboratory findings.

Discussion

In our study, we found that NLR and PLR values were significantly higher in patients with pediatric CSNHL than the healthy control group. There was no significant correlation between laboratory values and ABR test results. To the best of our knowledge, this is the first study to investigate NLR, PLR and MPV levels as

inflammatory biomarkers in patients with pediatric CSNHL. As far as the literature is concerned, we could not find a similar study.

The physiopathology of CSNHL could not be fully understood. Many factors, such as inflammation, genetic factors, environmental factors, and bacterial and viral infections, have been implicated in the etiopathogenesis of CSNHL [1-4]. Chronic inflammation may have a vital role in CSNHL physiopathology. Furthermore, many different cytokines secreted from inflammatory cells may play an important role in the physiopathogenesis of SNHL. Neutrophils, lymphocytes, and platelets are important blood elements involved in inflammatory processes. Cytokines involved in the pathogenesis of inflammatory processes are known to increase NLR [6-9]. Neutrophils secrete large amounts of inflammatory mediators and function as mediators of tissue destruction under inflammatory conditions [17]. Also, platelets play a role in inflammatory processes by affecting T lymphocytes, neutrophils, mononuclear phagocytes and endothelial cells [11,12]. According to recent studies, activated platelets can trigger inflammation [11,12].

Globally, NLR, PLR, and MPV values are being widely used as systemic inflammation and infection indicators. NLR, PLR, and MPV values are cheap and easy to calculate parameters. These parameters have been shown to increase in many diseases such as ISSNHL [5, 6], tinnitus [7], Bell palsy [8], vestibular neuritis [9], chronic otitis media with effusion [13], FMF [14], SLE [15] and cardiovascular diseases such as coronary artery diseases [16,17].

Seo et al. [5] found that NLR and PLR values were significantly higher in ISSNHL patients than in the control group, and they suggested that this indicates the presence of atherosclerosis in the pathogenesis of ISSNHL. Studies have shown that higher NLR values indicate a higher inflammation [22]. High neutrophils and NLR values have been implicated in causing increased damage to endothelial cells [23].

Another study suggests that NLR and MPV can be used to predict prognosis in patients with sudden hearing loss [6]. In patients with sudden hearing loss and high NLR, a decreased response to treatment has been seen, and this has been reported as a poor prognostic factor [6].

Ozbay et al. [7] reported significantly higher NLR values in patients with severe tinnitus than the control group. They argued that high NLR should be considered a potential clinical marker of tinnitus.

Bucak et al. [8] showed that neutrophil and NLR values were significantly higher in patients with Bell palsy than the control group. They also claimed that NLR could be used as a new potential marker for predicting the prognosis of patients while evaluating patients with Bell palsy.

Chung et al. [9] showed that NLR and PLR levels were significantly higher in patients with vestibular neuritis than in the healthy control group. They claimed that NLR and PLR values could be used as simple and reliable parameters to estimate the cause and severity of the disease.

Eryilmaz et al. [12] examined MPV, NLR, PLR and erythrocyte distribution width values in chronic otitis media children with or

without cholesteatoma. In this study, no statistically significant difference was found in the parameters other than MPV in both groups. Contrary to this, MPV values have been shown to be significantly lower in patients with cholesteatoma than in the control group [12]. To determine cholesteatoma in COM patients, it has been suggested that MPV level can be used as an independent predictor with high sensitivity and specificity [12].

In a study examining the relationship between chronic otitis media with effusion (COME) and NLR and PLR values, NLR was found to be significantly higher in the patient group compared to the control group [13]. The PLR parameter was found to be high in COME patients; however, it was not statistically significant. It has been claimed that NLR can be used as a diagnostic parameter in patients with COME [13].

In a study of cases with FMF, NLR values of patients with frequent attacks were found to be higher than those without attacks and healthy controls [14].

In a study, NLR, PLR, and MPV levels were found to be high in patients with Systemic Lupus Erythematosus (SLE) [15]. High NLR and PLR levels have been suggested to show a positive correlation with inflammatory markers and disease activity. It has been claimed that NLR and PLR levels, together with other serum inflammatory markers such as C-reaction protein and erythrocyte sedimentation rate, can be used as useful biomarkers in determining inflammatory response or disease activity in SLE patients [15]. NLR and PLR may reflect inflammatory response and disease activity in SLE patients.

It has been shown that WBC and its subtypes can be used as inflammatory markers in cardiovascular diseases [16,17]. It has been suggested that NLR value as an inflammatory marker may help predict prognosis in patients with acute coronary syndromes.

In other words, mortality has been shown to increase in patients with higher NLR values [16,17]. Furthermore, it has been suggested that parameters such as NLR and PLR are found to be high in various malignancies, and these high parameters are associated with poor prognosis [18-21].

Limitations

The presented study has some limitations. First, the sample size is relatively small, and all subjects are from the same center. Second, there are no long-term follow-up results. Third, a retrospective case study may not be accurate in nature due to the possibility that patient characteristics may not be fully recorded.

Conclusions

In conclusion, this study showed that NLR and PLR values in CSNHL patients were significantly higher compared to the control group. MPV values did not show a significant difference between the two groups. The findings of this study are generally consistent with the literature. To the best of our knowledge, the relationship between CSNHL and NLR and PLR has been demonstrated for the first time. Based on these data, it can be said that NLR and PLR values, which can be easily calculated at low cost, can be used as a suitable auxiliary parameter for the detection of inflammation in CSNHL patients. Further studies are needed to determine the

relationship between hearing loss etiopathogenesis and hearing loss levels and NLR, PLR, and MPV.

Competing interests

The authors have no financial conflicts of interest.

Financial Disclosure

The authors declared that this study has received no financial support.

Ethical approval

The study protocol was approved by the Ethics Committee of Harran University, School of Medicine (13.06.2019 / 06-38), and was conducted under the ethical principles described by the Helsinki Declaration.

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