Neurology Asia 2025; 30(3) : 871 – 879

Evaluation of systemic immune and inflammatory biomarkers in pediatric idiopathic intracranial hypertension patients

[1]Erel ICEL *MD*, [2]Hande GAZETECI TEKIN *MD*

[1]Bakırçay University Çiğli Training and Research Hospital, Faculty of Medicine, Department of Ophthalmology, Izmir, TURKEY; [2]Bakırçay University Çiğli Training and Research Hospital, Faculty of Medicine, Department of Pediatrics, Izmir, Turkey

Abstract

Background & Objective: Idiopathic intracranial hypertension (IIH) is characterized by increased intracranial pressure with normal cerebrospinal fluid analysis and neuroimaging findings. The aim of this study is to evaluate the relationship between systemic immune-inflammation index (SII) (neutrophil*platelet/lymphocyte count) and systemic inflammation response index (SIRI) (monocyte*neutrophil/lymphocyte count) as inflammatory markers with IIH in pediatric patients. *Methods:* A total of 42 eyes from 21 pediatric patients diagnosed with IIH and 42 eyes from 21 control subjects were included in the study. Macular and peripapillary measurements, neutrophil/lymphocyte ratio (NLR), monocyte/lymphocyte ratio (MLR), platelet/lymphocyte ratio (PLR), SII, and SIRI were recorded. *Results:* The study included groups matched for age and gender. When comparing inflammatory parameters, significantly higher values were observed in individuals with IIH for NLR ($P < 0.001$), PLR ($P = 0.005$), SII ($P < 0.001$), and SIRI ($P < 0.016$). In the univariate analysis of inflammatory parameters, NLR, PLR, MLR, SII, and SIRI values were identified as potential markers for IIH ($P = 0.001$, $P < 0.001$, $P = 0.004$, $P = 0.004$, $P = 0.001$, respectively). In the multivariate logistic regression analysis, NLR and PLR values were significantly higher (NLR: OR=3.8, 95% confidence interval [CI]: 1.3-11.0, P=0.013; PLR: OR=6.0, 95% CI: 1.7-20.8, P=0.005). Significant differences were found in mean retinal nerve fiber layer thickness (RNFLT) values between the two groups on OCT ($p<0.001$). Significant differences were also detected in ganglion cell layer thickness values between the two groups ($p=0.003$).
Conclusion: Multivariate logistic regression analysis suggests that NLR and PLR values could be effectively used in the diagnosis and treatment of the disease. No statistically significant differences were found between groups in SII and SIRI values.

Keywords: Idiopathic intracranial hypertension, monocyte-lymphocyte ratio, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation response index

INTRODUCTION

Idiopathic intracranial hypertension (IIH) is a neurological condition characterized by increased intracranial pressure, typically with normal cerebrospinal fluid analysis and neuroimaging findings. Symptoms commonly include headaches, visual disturbances, and pulsatile tinnitus. Typical ocular manifestations include papilledema, visual impairment, and visual field defects.[1,2] IIH is a relatively common disease in the pediatric population. Identifying and diagnosing IIH in children can be challenging. Factors such as limited compliance with examinations, variability in clinical signs and symptoms, and the difficulties associated with diagnostic investigations, which frequently necessitate general anesthesia or sedation, contribute to these challenges.[3] Neurological examination is normal except for findings of 6th cranial nerve palsy, papilledema, and vision loss.[4] The pathogenesis of IIH remains unclear, but there are three possible mechanisms that could alter cerebrospinal fluid (CSF)

Address correspondence to: Erel ICEL, MD, Assoc. Prof., Bakırçay University Çiğli Training and Research Hospital, Faculty of Medicine, Department of Ophthalmology, Izmir, TURKEY. Telephone: +90 (232) 3983700, E-mail: dr_erel@hotmail.com

Date of Submission: 14 March 2025; Date of Acceptance: 28 April 2025

https://doi.org/10.54029/2025kre

physiology: CSF hypersecretion, CSF outflow obstruction, and increased venous sinus pressure. Researchers have also considered metabolic and hormonal factors, as well as genetics.[5-8] There are several studies that found evidence of the role of low-grade inflammation in IIH, particularly in obese females.[9,10] The inflammatory response involves the coordinated activation of signaling pathways that regulate levels of inflammatory mediators in resident tissue cells and inflammatory cells, such as neutrophils, macrophages, and lymphocytes recruited from the blood. A complete blood count, as a simple, easy, and inexpensive examination, can reflect the inflammatory state. The absolute counts of white blood cells (WBC), neutrophils, monocytes, lymphocytes, and specific inflammation markers derived from these cells can serve as reliable indicators of systemic inflammatory status. In numerous pathologies characterized by inflammation, inflammatory markers obtained from peripheral blood are now utilized as prognostic indicators and predictors of disease progression, including IIH.[11,12] Visual field (VF) testing and optical coherence tomography (OCT) are crucial tests for diagnosing and monitoring patients. Peripapillary OCT is extensively employed for diagnosing papilledema and significantly influences treatment decisions. Previous studies have demonstrated associations between retinal nerve fiber layer thickness (RNFLT) and intracranial pressure (ICP).[12,13]

To the best of our knowledge, the relationship between systemic immune and inflammatory biomarkers and IIH has not been investigated in the pediatric IIH patients. The aim of this study is to evaluate the relationship between various inflammatory markers, including the systemic immune-inflammation index (SII) (neutrophil*platelet/lymphocyte count) and systemic inflammation response index (SIRI) (monocyte*neutrophil/lymphocyte count), with papilledema and retinal nerve fiber analysis.

METHODS

This retrospective observational study was conducted in compliance with the principles outlined in the Declaration of Helsinki, following approval from the Non-Interventional Clinical Research Ethics Committee of Bakırçay University Çiğli Training and Research Hospital (Approval Number 1380/1360). Participants whose examinations were completed between April 2022 and February 2024 at the Departments of Ophthalmology and Pediatric Neurology of Bakırçay University Çiğli Training and Research Hospital were included in the study.

Subjects were included if the diagnosis of idiopathic intracranial hypertension was made before the age of 18 and if they met the modified Dandy criteria (Table 1).[14] Patients with refractive errors outside the range of +/- 3 diopters, those with any ocular/systemic disease other than IIH, those using medical treatment for any reason other than IIH, and those with poor quality OCT images (OCT signal strength <6) were not included in the study. Patients with vision loss excluded from study.

Clinical data

Variables recorded for each subject include age, gender, body mass index, opening pressure on lumbar puncture, magnetic resonance imaging (MRI) findings of elevated intracranial pressure (empty sella, globe flattening, prominent perioptic cerebrospinal fluid, venous sinus stenosis) and neurological symptoms. The results of complete blood count (CBC) analysis were documented. All participants' complete ophthalmological examination data, including Log-MAR-converted best-corrected visual acuity (BCVA), intraocular pressure (Canon TX20P (Tokyo, Japan)), slit-lamp biomicroscopy and non-dilated fundoscopy findings, and RNFLT analyses of both eyes were recorded. Additionally, for patients with papilledema, the Frisén scale was utilized for grading.[14-16]

RNFLT and GCLT measurement

The macular and peripapillary measurements were conducted with the Cirrus 5000 HD-OCT (Cirrus HD-OCT; Carl Zeiss Meditec, Dublin, CA). The Cirrus HD-OCT 5000 operates at a scanning velocity of 27,000 scans per second, offering a 5 μm axial resolution and a scanning depth of 2mm. The equipment employs light with a wavelength of 840 nm and conducts scans over a 6×6 mm area for both macula and disc examinations. Using the Cirrus HD-OCT, both optic disc and macular cubes were acquired. The optic disc cube comprises 200 B-scans, with each containing 200 A-scans. The global RNFLT and the RNFLT values of the superior, nasal, inferior, and temporal quadrants were recorded for each case. Furthermore, the mean thickness of the ganglion cell layer (GCLT) was calculated based on the analyses.

Table 1. Clinical criteria for diagnosing IIH

1– Criteria required for the diagnosis of IIH include:	2– Criteria for diagnosing IIH without papilledema:
a. Presence of papilledema b. Normal neurologic examination except for cranial nerve abnormalities c. Neuroimaging findings: Normal brain parenchyma without evidence of hydrocephalus, mass, or structural lesion; absence of abnormal meningeal enhancement on MRI with and without gadolinium for typical patients (female and obese); MRI with and without gadolinium, and magnetic resonance venography for others. If MRI is unavailable or contraindicated, contrast-enhanced CT may be used. d. Normal composition of cerebrospinal fluid (CSF) e. Elevated lumbar puncture opening pressure (>250 mm CSF in adults and >280 mm CSF in children [>250 mm CSF if the child is not sedated and not obese]) in a properly performed lumbar puncture.	a. If papilledema is absent, a diagnosis of IIH can still be made if criteria b-e from the above list are satisfied, and the patient has a unilateral or bilateral abducens nerve palsy. b. If papilledema or sixth nerve palsy is absent, a diagnosis of IIH cannot be made, but it can be suggested if criteria b-e from the above list are satisfied, and at least 3 of the following neuroimaging criteria are met: i. Empty sella ii. Flattening of the posterior aspect of the globe iii. Distention of the perioptic subarachnoid space with or without a tortuous optic nerve iv. Transverse venous sinus stenosis

Based on the revised 2013 diagnostic criteria (x) for IIH (idiopathic intracranial hypertension), utilizing MRI (magnetic resonance imaging), CT (computed tomography), and CSF (cerebrospinal fluid).

Laboratory testing

Blood samples were obtained from all participants after fasting. CBC measurements were conducted using an automated hematology analyzer. The ratios of neutrophil to lymphocyte count (NLR), monocyte to lymphocyte count (MLR), and platelet to lymphocyte count (PLR) were documented. SII was computed by multiplying the neutrophil count by the platelet count and then dividing by the lymphocyte count. Similarly, SIRI was calculated by multiplying the monocyte count by the neutrophil count and then dividing by the lymphocyte count.

Statistical analyses

The data analysis for this study was performed using IBM SPSS Statistics 26. The suitability of continuous variables for normal distribution was evaluated using graphical analysis, normality tests, and sample size considerations. It was concluded that the data did not meet the criteria for a normal distribution.

Continuous variables are presented as median IQR (25-75). Comparisons of independentgroups, was done with the Mann-Whitney U test. Effect sizes (Cohen-D value) were calculated. The cut-off value was calculated by performing ROC analysis. Categorical independent variables were presented in cross-tables as frequencies and percentages, their distributions were compared using the chi-square tests. Univariate and multivariate binary logistic regression analyses (backward stepwise – Wald method) were performed to identify the risk factors. Odds ratios with 95% confidence intervals were calculated for each. In all statistical comparison tests, the margin of type one error was determined as α:0.05 and two-tailed tests were performed.

RESULTS

This study included 42 eyes from 21 patients (14 females) diagnosed with IIH, as well as 42 eyes from 21 control (14 females) subjects, which were screened for analysis. Six eyes belonging to 3 patients with idiopathic intracranial hypertension (IIH) and drusen were excluded from the study. The median age of individuals in the IIH group was 12 years old (interquartile range (IQR): 11–15), while the control was 11 years old (interquartile range (IQR): 10–13). All 21 patients newly diagnosed with IIH met the diagnostic criteria. Among the IIH group, 5 patients (24%) were

without papilledema, whereas 16 patients (76%) presented with papilledema. In the IIH group, the degrees of papilledema were as follows: 24% (n=10) grade 0, 50% (n=21) grade 1, 7% (n=3) grade 2, 10% (n=4) grade 3, and 10% (n=4) grade 4. In this group, 76% of patients experienced headaches, 14% had sixth cranial nerve palsy, 5% reported dizziness, and 5% had no symptoms. The median LP measurement in the IIH group was 52 cm H_2O, with an interquartile range (IQR) of 45–62. The demographic data and clinical characteristics of the study subjects are outlined in Table 2. This table also includes participants' blood and OCT parameters. As indicated in Table 2, individuals within the IIH group exhibited notably elevated values for NLR ($P < 0.001$), PLR ($P = 0.005$), SII ($P < 0.001$), and SIRI ($P < 0.016$).

ROC analysis was performed to assess the predictive capacity of the biomarkers for IIH. Based on the area under the curve (AUC) values, NLR (AUC: 0.721, 95% CI: 0.613-0.813), PLR (AUC: 0.67, 95% CI: 0.559-0.769), SII (AUC: 0.721, 95% CI: 0.613-0.813), and SIRI (AUC: 0.65, 95% CI: 0.538-0.751) demonstrated superior predictive capability for IIH patients compared to MLR (AUC: 0.586, 95% CI: 0.473-0.693). There was no statistical difference observed for the MLR value. Details of the optimal cut-off, specificity and sensitivity rates are shown in Table 3.

The cut-off values for all parameters are detailed in Table 4 along with chi-square tests. Thus, as known, the validity of the cut-off values has been verified. Logistic regression models for the participants are presented in Table 5. The univariate analysis of inflammatory parameters revealed that NLR, PLR, MLR, SII, and SIRI values could serve as markers for IIH ($p=0.001$, $p<0.001$, $p=0.004$, $p=0.004$, $p=0.001$, respectively). When these values were included in the multivariate analysis, NLR and PLR values were found to be significant. In the multivariate logistic regression analysis, the admission NLR and PLR values remained significant (NLR: OR=3.8, 95% confidence interval [CI]: 1.3-11.0, P=0.013; PLR: OR=6.0, 95% confidence interval [CI]: 1.7-20.8, P=0.005). Baseline variables that showed significant variations were included in the logistic regression analyses.

When evaluating the OCT measurements, a significant difference was found in the average RNFL values between the two groups ($p<0.001$). A

Table 2: Demographic data, hematological parameters and OCT measurements of the study participants

	IIH Med (IQR)	**Control** Med (IQR)	P_{Value}*	d_{Cohen}
Gender (Female). N (%)	28 (66.7%)	28 (66.7%)	1.000**	0.00
Age. (yr)	12 (11 – 15)	11 (10 – 13)	0.302	0.22
BMI (kg/m^2)	31 (23 – 34)	18 (16 – 19)	**<0.001**	2.17
Neutrophil (10^3 /µL)	4.7 (2.6 – 6.9)	3.5 (2.9 – 4.0)	**0.041**	0.46
Platelet (10^3 /µL)	312 (261 – 361)	286 (265 – 320)	**0.046**	0.45
Lymphocyte (10^3 /µL)	2.26 (1.64 – 2.72)	2.68 (2.32 – 2.92)	**0.005**	0.64
Monocyte (10^3 /µL)	0.5 (0.32 – 0.70)	0.51 (0.41 – 0.75)	0.830	0.05
NLR	1.74 (1.18 – 3.08)	1.25 (0.97 – 1.64)	**<0.001**	0.82
PLR	133 (96 – 201)	111 (91 – 132)	**0.007**	0.61
MLR	0.22 (0.14 – 0.32)	0.22 (0.13 – 0.26)	0.173	0.30
SII	552 (361 – 1022)	345 (257 – 492)	**<0.001**	0.82
SIRI	0.91 (0.53 – 1.78)	0.65 (0.43 – 0.88)	**0.018**	0.53
GCLT	85 (83 – 86)	87 (85 – 89)	**0.003**	0.69
RNFLT Mean (µm)	105 (96 – 111)	95 (92 – 102)	**<0.001**	0.84
RNFLT Superior (µm)	128 (117 – 152)	123 (115 – 133)	0.079	0.39
RNFLT Nasal (µm)	76 (68 – 90)	66 (60 – 72)	**<0.001**	0.77
RNFLT Inferior (µm)	136 (127 – 154)	133 (116 – 142)	**0.025**	0.50
RNFLT Temporal (µm)	65 (60 – 75)	64 (61 – 70)	0.989	0.00

*Mann-Whitney Test. **Pearson Chi-Square Test. Med:Median. IQR:Interquartile range (25-75). d-Cohen: Effect Size [d value (0.0-0.1 No Effect. 0.2-0.4 Small Effect. 0.5-0.7 Intermediate Effect. ≥ 0.8 Large Effect)]

BMI: body mass index, NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, MLR: monocyte to lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammation response index, RNFLT: retinal nerve fiber layer thickness, GCLT: ganglion cell layer thickness

Table 3: Findings of ROC Analysis and Sensitivity, Specificity Values in IIH

Variable	AUC (95% CI)	$P_{(Area=0.5)}$	$J_{Youden\ index}$	Cut Off Value	Sensitivity	Specificity
BMI (kg/m2)	0.927 (0.850 – 0.973)	<0.001	0.810	>22	81	100
Neutrophil (10^3 /μL)	0.629 (0.517 – 0.732)	0.057	0.429	>4.48	52	90
Platelet (10^3 /μL)	0.626 (0.514 – 0.730)	0.050	0.333	>299	71	62
Lymphocyte (10^3 /μL)	0.678 (0.567 – 0.776)	0.002	0.286	≤1.64	29	100
Monocyte (10^3 /μL)	0.514 (0.402 – 0.624)	0.833	0.143	≤0.82	86	0
NLR	0.721 (0.613 – 0.813)	<0.001	0.381	>1.66	57	81
PLR	0.67 (0.559 – 0.769)	0.005	0.381	>140	48	90
MLR	0.586 (0.473 – 0.693)	0.176	0.286	>0.3	33	95
SII	0.721 (0.613 – 0.813)	<0.001	0.429	>714	43	100
SIRI	0.65 (0.538 – 0.751)	0.016	0.381	>1.34	43	95
GCLT	0.689 (0.578 – 0.785)	0.001	0.381	≤86	79	60
RNFLT Mean (μm)	0.726 (0.617 – 0.817)	<0.001	0.405	>99	71	69
RNFLT Superior (μm)	0.611 (0.499 – 0.716)	0.076	0.31	>140	31	100
RNFLT Nasal (μm)	0.709 (0.600 – 0.803)	<0.001	0.405	>74	55	86
RNFLT Inferior (μm)	0.642 (0.530 – 0.743)	0.019	0.286	>152	29	100
RNFLT Temp. (μm)	0.501 (0.390 – 0.612)	0.990	0.143	>74	26	88

BMI: body mass index, NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, MLR: monocyte to lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammation response index, RNFLT: retinal nerve fiber layer thickness, GCLT: ganglion cell layer thickness

detailed examination of the RNFL measurements is shown in Figure 1. There was a significant difference in the ganglion cell layer thickness values between the two groups (p=0.003) (Figure 2).

DISCUSSION

This retrospective observational study aimed to investigate the utility of NLR, PLR, MLR, SII and SIRI as biomarkers of inflammation. In this study, the findings indicated elevated neutrophil and platelet counts, as well as increased NLR and PLR in pediatric patients diagnosed with IIH. These parameters, derived from a routine CBC test, serve as inflammatory markers and were notably higher in the IIH patient group compared to controls. To our knowledge, no study has previously reported markers for the identification of IIH in pediatric patients.

Indeed, the role of inflammation in the pathogenesis of IIH has been a subject of investigation in numerous studies though the exact mechanisms linking inflammation to IIH remain complex and multifactorial.[9-12]

Sinclair *et al*. observed significantly higher levels of CSF leptin in IIH compared to controls matched for age, gender, and body mass index (BMI). Leptin is a hormone primarily produced by adipose tissue and plays a role in regulating appetite and energy balance. Elevated levels of leptin in CSF suggest a potential link between adipose tissue function, metabolism, and the pathophysiology of IIH, possibly contributing to the dysregulation of intracranial pressure through its effects on appetite regulation, metabolism, and potentially inflammatory processes within the central nervous system.[17] Numerous studies have demonstrated the involvement of low-grade inflammation in IIH, especially among obese female patients.[9,12] In this study, BMI values in the IIH group were found to be significantly higher than those in the control group. Although previous studies have found that obesity increases inflammatory markers, in this article only NLR and PLR ratios were found to be elevated, and no significant differences were detected in MLR, SII and SIRI values.

Dhungana *et al.* reported elevated CSF leptin, IL-1α (Interleukin-1 alpha), and CCL2 (Chemokine ligand 2, also known as MCP-1) in the CSF of IIH patients.[18] Samancı *et al.* demonstrated that increased IL-1β and decreased IL-8 and TNFα may play a crucial role in the

Table 4: The cutoff values for hematological parameters and OCT measurements of the study participants

		IIH n(%)	Control n(%)	P*	d Cohen
BMI	>22	34 (81%)	0 (0%)	**<0.001**	0.00
	≤22	8 (19%)	42 (100%)		
Neutrophil	>4.48	22 (52%)	4 (10%)	**<0.001**	2.67
	≤4.48	20 (48%)	38 (90%)		
Platelet	>299	30 (71%)	16 (38%)	**0.004**	0.65
	≤299	12 (29%)	26 (62%)		
Lymphocyte	≤1.64	12 (29%)	0 (0%)	**0.001**	0.81
	>1.64	30 (71%)	42 (100%)		
Monocyte	≤0.82	36 (86%)	42 (100%)	**0.026**	0.48
	>0.82	6 (14%)	0 (0%)		
NLR	>1.66	24 (57%)	8 (19%)	**0.001**	0.79
	≤1.66	18 (43%)	34 (81%)		
PLR	>140	20 (48%)	4 (10%)	**<0.001**	0.86
	≤140	22 (52%)	38 (90%)		
MLR	>0.3	14 (33%)	2 (5%)	**0.002**	0.71
	≤0.3	28 (67%)	40 (95%)		
SII	>714	18 (43%)	0 (0%)	**<0.001**	1.13
	≤714	24 (57%)	42 (100%)		
SIRI	>1.34	18 (43%)	2 (5%)	**<0.001**	0.92
	≤1.34	24 (57%)	40 (95%)		
GCLT	≤86	33 (79%)	17 (40%)	**0.001**	0.78
	>86	9 (21%)	25 (60%)		
RNFLT (Mean)	>99	30 (71%)	13 (31%)	**<0.001**	0.82
	≤99	12 (29%)	29 (69%)		
RNFLT (Superior)	>140	13 (31%)	0 (0%)	**<0.001**	0.86
	≤140	29 (69%)	42 (100%)		
RNFLT (Nasal)	>74	23 (55%)	6 (14%)	**<0.001**	0.87
	≤74	19 (45%)	36 (86%)		
RNFLT (Inferior)	>152	12 (29%)	0 (0%)	**0.001**	0.81
	≤152	30 (71%)	42 (100%)		
RNFLT (Temporal)	>74	11 (26%)	5 (12%)	0.165	0.31
	≤74	31 (74%)	37 (88%)		

*Pearson Chi-Square Test. d-Cohen: Effect Size

BMI: body mass index, NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, MLR: monocyte to lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammation response index, RNFLT: retinal nerve fiber layer thickness, GCLT: ganglion cell layer thickness

prognosis and possibly the pathophysiology of IIH.[10]

Indeed, NLR and PLR have been extensively studied and recognized as inflammation markers across a wide range of chronic conditions and diseases.[19-21] SIRI is recognized as a comprehensive marker for chronic low-grade inflammation, utilizing counts of monocytes, neutrophils, and lymphocytes. Elevated SIRI levels have been identified as significant prognostic and predictive factors in various medical conditions.[22-25]

This study provides evidence supporting the concept of intracranial hypertension as an inflammatory process. Notably, it highlights a straightforward and adjunctive approach for assessing intracranial hypertension in cases where an invasive procedure, such as lumbar puncture, is being considered but a definitive preliminary

Table 5: Results of univariate and multivariate logistic regression analyses identifying risk factors influencing the prediction of IIH

	Univariate		Multivariate*		
	OR (95%CI)	**P**	**OR (95%CI)**	**P**	
BMI [>22/≤22]	345 (19 – 6191)	**<0.001**	—	ni	Model I
Neutrophil [>4.48/≤4.48]	10 (3.2 – 35)	**<0.001**	8.3 (2.5 – 28.4)	**<0.001**	
Platelet [>299/≤299]	4.1 (1.6 – 10.1)	**0.003**	2.9 (1.1 – 7.8)	**0.039**	
Lymphocyte [≤1.64/>1.64]	35 (2 – 611)	**0.015**	—	ns	
Monocyte [≤0.82/>0.82]	0.07 (0 – 1.21)	0.067	—	ns	
NLR [>1.66/≤1.66]	5.7 (2.1 – 15.1)	**0.001**	3.8 (1.3 – 11.0)	**0.013**	Model II
PLR [>140/≤140]	8.6 (2.6 – 28.5)	**<0.001**	6.0 (1.7 – 20.8)	0.005	
MLR [>0.3/≤0.3]	10 (2.1 – 47.5)	**0.004**	—	ns	
SII [>714/≤714]	64 (3.7 – 1113)	**0.004**	—	ns	
SIRI [>1.34/≤1.34]	15 (3.2 – 70.4)	**0.001**	—	ns	
GCLT [≤86/>86]	5.4 (2.1 – 14.1)	**0.001**	10.0 (2.9 – 34.4)	**<0.001**	Mod III
RNFLT (Mean) [>99/≤99]	5.6 (2.2 – 14.2)	**<0.001**	10.1 (3.0 – 33.6)	**<0.001**	
RNFLT (Superior) [>140/≤140]	39 (2.2 – 680)	**0.012**	—	ns	Model IV
RNFLT (Nasal) [>74/≤74]	7.3 (2.5 – 20.9)	**<0.001**	7.3 (2.5 – 20.9)	**0.001**	
RNFLT (Inferior) [>152/≤152]	35 (2 – 611)	**0.015**	—	ns	
RNFLT (Temporal) [>74/≤74]	2.6 (0.8 – 8.4)	0.103	—	ni	

*Logistic Regression Method Backward Stepwise (Wald). ni = not included (if univar p>0.100 or dependent), ns = not significant, OR = odds ratio

NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, MLR: monocyte to lymphocyte ratio, SII: systemic immune-inflammation index, SIRI: systemic inflammation response index, RNFLT: retinal nerve fiber layer thickness, GCLT: ganglion cell layer thickness

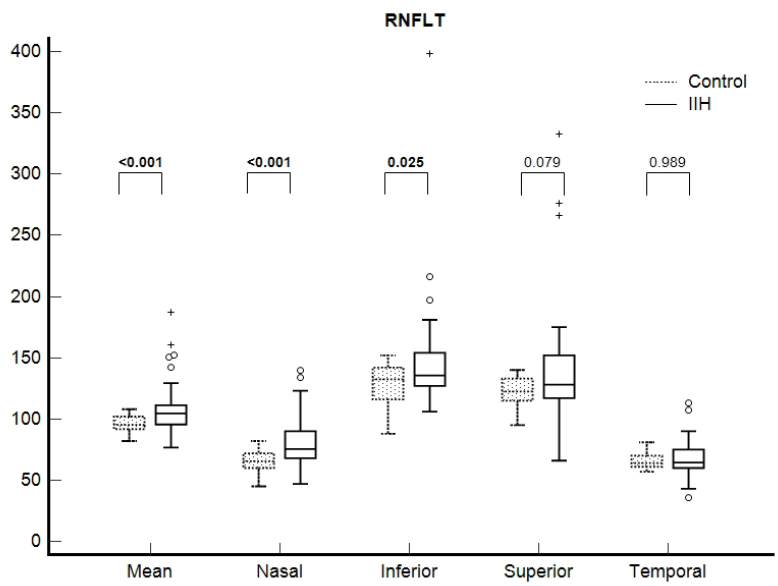

Figure 1. Comparison of RNFLT measurements between groups.

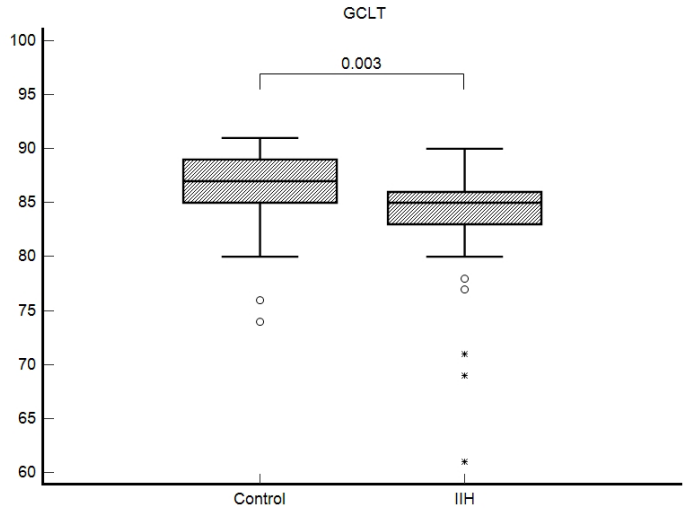

Figure 2. Comparison of GCLT measurements between groups.

diagnosis remains uncertain. Additionally, despite minimal optic nerve head changes observed during fundus examination in the early stages of IIH, the increase in RNFLT allows for diagnostic support through a non-invasive approach. In this study, we found that the mean RNFLT and nasal RNFLT levels were significantly higher in patients with predominantly early-stage papilledema compared to the control group. Accordingly, inflammatory markers such as NLR and PLR may serve as easily accessible adjunctive parameters in the diagnosis of IIH, alongside RNFLT measurements.

In multivariate analyses, the significantly elevated NLR and PLR ratios in children diagnosed with IIH may be influenced by various comorbid conditions, such as obesity and inflammatory disorders. Hormonal imbalances such as those observed in polycystic ovary syndrome (PCOS) and the use of exogenous anabolic steroids—both recognized among the secondary causes of intracranial hypertension—have been shown to affect systemic inflammatory responses. Several studies have reported alterations in inflammatory markers, particularly the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), in such endocrine conditions.[26] However, it remains controversial whether these changes represent a causal factor in the development of elevated intracranial pressure or are merely a consequence of it. Nonetheless, due to their accessibility and non-invasive nature, these inflammatory indices may serve as supportive biomarkers in patients who possess known risk factors and exhibit clinical suspicion of intracranial hypertension, even if they do not fully meet the diagnostic criteria. In this study, children with additional diagnoses that could potentially affect these ratios were excluded. Nevertheless, the inflammatory response may be elevated due to a slowly progressing disease that was overlooked or difficult to detect during the initial assessment in terms of IIH risk factors. However, the applicability of this approach in clinical practice may be limited.

This study has several limitations. The first limitation is related to the retrospective design. Additionally, while age and gender were matched between groups, BMI values were higher in the IIH group due to the nature of the disease compared to the control group. Furthermore, in most participants with existing papilledema in IIH, early-stage grade was present, thus no comparison could be made based on papilledema grade.

In conclusion, NLR and PLR, readily accessible markers of inflammation, were elevated in patients with IIH, suggesting that inflammation likely plays a significant role in the development of this disorder. Additional research using prospective designs is necessary to explore how NLR and PLR correlate with other inflammatory markers, including cytokines and chemokines, in both serum and CSF. This will help validate the role of inflammation in IIH.

DISCLOSURE

Data availability: The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Ethics: Written informed consent was obtained from all individual participants included in the study.

Financial support: None

Conflict of interest: None

REFERENCES

1. Blanch RJ, Vasseneix C, Liczkowski A, *et al*. Differing presenting features of idiopathic intracranial hypertension in the UK and US. *Eye* (Lond) 2019; 33:1014-9. https://doi.org/10.1038/S41433-019-0359-5
2. Peralta GM, Cestari DM. An update of idiopathic intracranial hypertension. *Curr Opin Ophthalmol* 2018; 29:495-502. https://doi.org/10.1097/ICU.0000000000000518
3. Perri A, Rago V, Malivindi R, *et al*. Paediatric idiopathic intracranial hypertension (IIH)-A review. *Life* (Basel) 2021; 11:. https://doi.org/10.3390/LIFE11070632
4. Yamamoto E, Farber D, Rothner D, Moodley M. Assessment of pediatric pseudotumor cerebri clinical characteristics and outcomes. *J Child Neurol* 2021; 36:341-9. https://doi.org/10.1177/0883073820972231
5. Ko MW, Chang SC, Ridha MA, *et al*. Weight gain and recurrence in idiopathic intracranial hypertension: a case-control study. *Neurology* 2011; 76:1564-7. https://doi.org/10.1212/WNL.0B013E3182190F51
6. Daniels AB, Liu GT, Volpe NJ, *et al*. Profiles of obesity, weight gain, and quality of life in idiopathic intracranial hypertension (pseudotumor cerebri). *Am J Ophthalmol* 2007; 143:. https://doi.org/10.1016/J.AJO.2006.12.040
7. Sugerman HJ, Felton WL, Sismanis A, *et al*. Gastric surgery for pseudotumor cerebri associated with severe obesity. *Ann Surg* 1999; 229:634-42. https://doi.org/10.1097/00000658-199905000-00005
8. Kuehn MH, Mishra R, Deonovic BE, *et al*. Genetic survey of adult-onset idiopathic intracranial hypertension. *J Neuroophthalmol* 2019; 39:50-5. https://doi.org/10.1097/WNO.0000000000000648
9. Sinclair AJ, Ball AK, Burdon MA, *et al*. Exploring the pathogenesis of IIH: an inflammatory perspective. *J Neuroimmunol* 2008; 201-202:212-220. https://doi.org/10.1016/J.JNEUROIM.2008.06.029
10. Samancl B, Samancl Y, Tüzün E, *et al*. Evidence for potential involvement of pro-inflammatory adipokines in the pathogenesis of idiopathic intracranial hypertension. *Cephalalgia* 2017; 37:525-31. https://doi.org/10.1177/0333102416650705
11. Üçer MB, Cevher S. Assessment of systemic inflammatory response index and other inflammatory indicators in retinal vein occlusion. *Medicine* 2023; 102:E36512. https://doi.org/10.1097/MD.0000000000036512
12. Ceylan O, Yilmaz M, Yilmaz H, *et al*. Neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios as inflammation markers in patients with papilledema due to idiopathic intracranial hypertension. *Indian J Ophthalmol* 2021; 69:1499-505. https://doi.org/10.4103/IJO.IJO_2030_20
13. Skau M, Yri H, Sander B, *et al*. Diagnostic value of optical coherence tomography for intracranial pressure in idiopathic intracranial hypertension. Graefes *Arch Clin Exp Ophthalmol* 2013; 251:567-74. https://doi.org/10.1007/S00417-012-2039-Z
14. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. *Neurology* 2013; 81:1159-65. https://doi.org/10.1212/WNL.0B013E3182A55F17
15. Frisen L Swelling of the optic nerve head: a staging scheme. *J Neurol Neurosurg Psychiatry* 1982; 45:13-8. https://doi.org/10.1136/JNNP.45.1.13
16. Sinclair AJ, Burdon MA, Nightingale PG, *et al*. Rating papilloedema: an evaluation of the Frisén classification in idiopathic intracranial hypertension. *J Neurol* 2012; 259:1406-12. https://doi.org/10.1007/S00415-011-6365-6
17. Sinclair AJ, Ball AK, Curnow SJ, *et al*. Elevated cerebrospinal fluid (CSF) leptin in idiopathic intracranial hypertension (IIH): evidence for hypothalamic leptin resistance? *Clin Endocrinol* (Oxf) 2009; 70:863-9. https://doi.org/10.1111/J.1365-2265.2008.03401.X
18. Dhungana S, Sharrack B, Woodroofe N. Cytokines and chemokines in idiopathic intracranial hypertension. *Headache* 2009; 49:282-5. https://doi.org/10.1111/J.1526-4610.2008.001329.X
19. Imtiaz F, Shafique K, Mirza S, *et al*. Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic diseases in Asian population. *Int Arch Med* 2012;5:2. https://doi.org/10.1186/1755-7682-5-2
20. Ozgonul C, Sertoglu E, Mumcuoglu T, Kucukevcilioglu M. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio as novel biomarkers of primary open-angle glaucoma. *J Glaucoma* 2016;25:e815–e820. https://doi.org/10.1097/IJG.0000000000000392
21. Icel E, Ucak T, Karakurt Y, *et al*. The relation of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio with high axial myopia. *Ocul Immunol Inflamm* 2020;28:396-401. https://doi.org/10.1080/09273948.2019.1588334
22. Zuo W, Chen T, Song J, Ai M. Assessment of systemic immune-inflammation index levels in patients with retinal vein occlusion. *Ocul Immunol Inflamm* 2023; 31:491-5. https://doi.org/10.1080/09273948.2022.2032199
23. Zhang Y, Xing Z, Zhou K, Jiang S. The predictive role of systemic inflammation response index (SIRI) in the prognosis of stroke patients. *Clin Interv Aging* 2021; 16:1997-2007. https://doi.org/10.2147/CIA.S339221
24. Han K, Shi D, Yang L, *et al*. Prognostic value of systemic inflammatory response index in patients with acute coronary syndrome undergoing percutaneous coronary intervention. *Ann Med* 2022;54:1667-77. https://doi.org/10.1080/07853890.2022.2083671
25. Xu Y, He H, Zang Y, *et al*. Systemic inflammation response index (SIRI) as a novel biomarker in patients with rheumatoid arthritis: a multi-center retrospective study. *Clin Rheumatol* 2022; 41:1989-2000. https://doi.org/10.1007/S10067-022-06122-1
26. Gao Z, Liu K. Association between systemic immunity-inflammation index and sex hormones in children and adolescents aged 6-19. *Front Endocrinol* (Lausanne) 2024; 15:1355738. https://doi.org/10.3389/FENDO.2024.1355738