RESEARCH ARTICLE

INDONESIAN JOURNAL OF CANCER

The Correlation of Inflammatory Markers with Clinical Manifestation, Peritumoral Edema, and Recurrence in Meningioma Patients

Tiara Aninditha [1*], Putri Auliya [1], Rahmad Mulyadi [2], Renindra Ananda Aman [3], Rini Andriani [4], Henry Riyanto Sofyan [1]

[1] Department of Neurology, Medical Faculty of Indonesia University, Jakarta, Indonesia
[2] Department of Radiology, Medical Faculty of Indonesia University, Jakarta, Indonesia
[3] Department of Neurosurgery, Medical Faculty of Indonesia University, Jakarta, Indonesia
[4] Department of Neurology, National Dharmais Cancer Hospital, Jakarta, Indonesia

ARTICLE INFO

Received : 02 August 2024
Revised : 08 October 2024
Accepted : 31 October 2024
Published : 30 June 2025

Keywords:
edema, inflammatory, markers, meningioma, recurrence

*Corresponding Author:
Tiara Aninditha
Department of Neurology, Medical Faculty of Indonesia University, Jakarta, Indonesia
t.aninditha@ui.ac.id

ABSTRACT

Background: Meningiomas can induce inflammation in their tumorigenesis process, thereby linking inflammation with clinical symptoms, peritumoral edema, and recurrence of meningiomas. Easily accessible and cost-effective inflammatory markers include the neutrophil-lymphocyte ratio (NLR) and monocyte-lymphocyte ratio (MLR). This study aims to investigate the relationship between peripheral inflammation markers, specifically the NLR and MLR, and their association with clinical symptoms, peritumoral edema, and meningioma recurrence.

Method: A retrospective cohort study was conducted at Cipto Mangunkusumo National General Hospital from January 2016 to December 2019, utilizing a consecutive non-probability sampling method. Inclusion criteria were patients aged 18 years or older with meningiomas (grades I-III), first surgery. Peripheral inflammatory markers were derived from differential blood counts, peritumoral edema data from radiological reports, and other data from medical records. The cut-off values for NLR and MLR were determined to be 2.415 and 0.295, respectively. Bivariate analyses using Chi-Square and Mann-Whitney tests were followed by multivariate logistic regression analysis.

Results: 173 patients were eligible for analysis. Of these, 27 had preoperative CT scans, 126 had MRIs, and 20 had no preoperative radiology data. Clinical and recurrence analyses were performed on all 173 patients, with radiology and tumor size analyses conducted on subsets of 153 and 126 patients, respectively. The majority of meningiomas in this study were grade I, found in 94.2% of subjects, with the remainder being grade II and III. Higher NLR and MLR values were significantly associated with headaches ($p < 0.001$). Elevated NLR and MLR were also correlated with peritumoral edema ($p < 0.001$). MLR was independently associated with recurrence, with an adjusted odds ratio (aOR) of 12.647 (95% CI 2.355–67.919); $p = 0.003$.

Conclusion: NLR and MLR as peripheral inflammatory markers demonstrated higher median values in meningioma patients with headaches and peritumoral edema. Additionally, inflammation in meningiomas was associated with the occurrence of recurrence.

INTRODUCTION

Meningiomas are the second most common primary brain tumors after gliomas. At Cipto Mangunkusumo National General Hospital (RSCM), meningiomas account for 26% of all primary central nervous system tumors [1]. Meningiomas exhibit a high tendency for recurrence [2,3]. In determining prognosis, recurrence presents a unique challenge in managing meningiomas [2,4]. Recurrence occurs in 50% of grade II meningiomas and

up to 90% in grade III meningiomas [3]. Additionally, meningiomas are generally asymptomatic, with clinical symptoms appearing gradually due to slow tumor growth, often resulting in patients being unaware until the clinical condition becomes severe. The clinical course and prognosis of meningiomas can be influenced by several factors, including initial tumor size, tumor shape, location, peritumoral edema, histology, extent of resection, progesterone receptor status, mitotic index (Ki67), growth factors, and immunohistochemical reactions [2,4].

According to the hallmarks of cancer, tumors possess the ability to induce inflammation, playing a crucial role in tumor initiation, growth, and therapy, and thus, in tumorigenesis [1,5]. Meningiomas also exhibit this inflammatory capability in their tumorigenesis process. Being located outside the blood-brain barrier, the inflammatory profile of meningiomas is more evident in peripheral blood compared to other brain tumors located within the brain parenchyma. This is evidenced by higher levels of C-reactive protein (CRP) in meningiomas compared to other intra-axial brain tumors, even though meningiomas generally have a lower grade [6,7].

Since inflammation is associated with tumor formation, it is also linked to clinical symptoms, peritumoral edema, and meningioma recurrence. This occurs due to the stimulation of nociceptors, causing headaches, angiogenesis associated with peritumoral edema, and tumorigenesis, increasing the risk of recurrence.

Inflammatory markers can predict clinical outcomes, progression, and recurrence, providing clinicians with a basis for estimating follow-up frequency in meningioma patients. This also reduces the need for expensive modalities. Furthermore, inflammatory markers can predict clinical outcomes pre- and post-tumor resection surgery, aiding neurologists in deciding on the use of anti-inflammatory treatments for meningiomas with clinical symptoms, edema, or recurrence. Easy and inexpensive inflammatory markers include the neutrophil-lymphocyte ratio (NLR) and the monocyte-lymphocyte ratio (MLR).

By investigating the relationship between NLR, MLR, and these dependent variables, the study aims to clarify the role of peripheral inflammatory markers in predicting the clinical course of meningioma patients, including symptom development, edema formation, and the likelihood of recurrence. The findings could potentially inform clinical decisions regarding follow-up and treatment strategies.

METHODS

This study is a retrospective cohort study utilizing secondary data from medical records of patients with meningiomas from January 2016 to December 2019. Sample selection was conducted using a non-probability consecutive sampling method. Inclusion criteria were patients aged 18 years or older, with anatomical pathology results indicating meningiomas (grades I, II, and III), who underwent their first meningioma surgery, and had complete laboratory and radiology data. Exclusion criteria included patients with comorbidities, other extracranial tumors, steroid use before blood sampling, postoperative patients who underwent surgery for one year or less, prior local radiotherapy before tumor resection, smoking, patients with re-craniotomy tumor removal, and incomplete medical records. The sample size was calculated using the formula for determining the Area Under the Curve (AUC) in diagnostic test analysis to accurately evaluate the predictive performance of the NLR and MLR in meningioma recurrence.

From the data of meningioma patients at RSCM from 2016 to 2019, A total of 289 patients aged 18 and older were identified. Of these, 31 had recurrent cases, leaving 258 patients who had their first surgery during this period. After excluding 26 patients with incomplete laboratory data, 232 met the inclusion criteria. Among these, 36 had comorbidities or used dexamethasone prior to laboratory tests, 9 had no clinical data, 13 had leukocytosis, and 1 had leukopenia, resulting in 173 eligible subjects. Of the 173 subjects, 27 had only pre-operative CT scan data, 126 had pre-operative MRI data, and 20 had no pre-operative radiology data. Clinical analysis (headache, seizures, focal neurology deficits, motor disturbance, sensory disturbance, visual disturbance, and cranial nerve paresis) and recurrence analysis on factors influencing recurrence (tumor location, meningioma grade, peritumoral edema, tumor size, NLR, MLR and simpson grade) was conducted on 173 subjects, radiology analysis (edema, edema grade, tumor location, menigioma grade, and hyperostosis) on 153 subjects, and tumor size and edema index analysis on 126 subjects. The majority of meningiomas in this study were grade I, accounting for 94.2% (163 subjects), with the remainder 5.8% (10 subjects) being grade II and III.

Researchers recorded and identified study subjects based on all patients with anatomical pathology data of meningiomas at RSCM who met the study criteria. Data retrieval was performed manually and electronically through medical records. Tumor size and edema index were measured using PACS. Data analysis was conducted in three stages: descriptive analysis, normality tests, correlation tests, and multivariate analysis. Numerical data with normal distribution were described as mean and standard deviation, while both normal and non-normally distributed numerical data were described as median and range. Categorical data were described in numbers and percentages. Following normality tests, Pearson correlation tests were conducted for normally distributed numerical variables, and Spearman tests were used for non-normally distributed numerical and ordinal variables. Odds ratio calculations using Cox regression (bivariate and multivariate analyses) were also performed. Receiver Operating Characteristic (ROC) analysis was used

P-ISSN: 1978-3744 E-ISSN: 2355-6811

to determine the optimal cut-off points for the NLR and MLR in predicting meningioma recurrence. All data were processed using SPSS version 25.

RESULTS

The average age of the subjects was 46.98 ± 8.26 years, with the majority aged 40-49 years (49.1%) and predominantly female (91.9%). There were 12 subjects (6.9%) with recurrence. Follow-up duration for the entire sample was 0-24 months, with 12 subjects (6.9%) experiencing early recurrence.

Based on **Table 1**, among the clinical characteristics of the study subjects, headaches were the most common symptom, affecting 64.7% of subjects. Among all focal clinical symptoms, visual disturbances were the most common, affecting 59% of subjects. Seizures were reported in 12.1% of subjects. Laboratory characteristics showed a median NLR of 2.37 (0.72–9.73) and a median MLR of 0.24 (0.11–0.94). Tumor characteristics revealed that the tumor location was more frequently at the skull base compared to the convexity, with 72.3% and 27.7%, respectively.

Among 143 subjects with preoperative MRI and CT scan images, 53.1% exhibited edema. Tumor size and edema index were measured in 126 subjects. The median edema index was 0.08, and the median tumor size was 192.73 cm^3. The majority of the subjects had grade I meningiomas (94.2%). Histopathologically, mixed histology was more common, with meningothelial cells being dominant (87.3%), followed by microcystic (31.2%) and transitional (26%).

Table 1. Demographic and clinical characteristics (n=173)

Variable	n (%)
Gender	
Female	159 (91.9)
Male	14 (8.1)
Age	
Mean ± SD	46.98 ± 8.26
18–29 years	7 (4)
30–39 years	19 (11)
40–49 years	85 (49.1)
50–59 years	51 (29.5)
> 60 years	11 (6.4)
Recurrence	
Yes	12 (6.9)
No	161 (93.1)
Follow-up duration (months)	
Median (min-max)	6 (0–24)
Clinical symptoms	
Headache	
Yes	112 (64.7)
No	61 (35.3)
Seizures	
Yes	21 (12.1)
No	152 (87.9)
Focal neurological deficits	
Yes	123 (71.1)
No	50 (28.9)
Motor disturbances	
Yes	20 (11.6)
No	153 (88.4)
Sensory disturbances	
Yes	3 (1.7)
No	170 (98.3)
Visual disturbances	
Yes	102 (59)
No	71 (41)
Cranial nerve paresis	
Yes	36 (20.8)
No	137 (79.2)
Laboratory	
NLR	
Median (min-max)	2.37 (0.72–9.73)
MLR	
Median (min-max)	0.24 (0.11–0.94)
Hemoglobin	
Mean ± SD	13.15 ± 1.21
Leukocytes	
Mean ± SD	8,450 ± 1,560
Tumor	
Tumor location	
Convexity	48 (27.7)
Skull base	125 (72.3)
Radiological characteristics	
Edema	
Yes	76 (53.1)
No	67 (46.9)
Edema index	
Median (min-max)	0.08 (0–10.6)
Tumor size	
Median (min-max)	192.73 (1.21–10.095)

P-ISSN: 1978-3744 E-ISSN: 2355-6811

Using the receiver operating characteristic (ROC) curve analysis, the optimal cut-off point for NLR in predicting meningioma recurrence was 2.415, with a sensitivity of 91.7% and a specificity of 55.3%. The area under the curve (AUC) for NLR was 0.692. The cut-off point for MLR was 0.295, with a sensitivity of 75% and a specificity of 78.3%, and an AUC of 0.806. These cut-off values will be used for subsequent correlation analysis in this study. As shown in **Table 2**, higher values of inflammatory markers (NLR and MLR) were associated with clinical headaches, with p < 0.001. Seizures, other neurological deficits, and recurrence were not

Table 2. Association between inflammatory markers and clinical and tumor characteristics of subjects (n = 173)

	NLR		P	OR (95% CI)	MLR		P	OR (95% CI)
	High	Low			High	Low		
Headache								
Yes	64 (37)	48 (27.2)	**< 0.001***	2.94 (1.526–5.694)	41 (23.7)	71 (41)	**< 0.001***	11.16 (3.28–37.91)
No	19 (11)	42 (24.3)			3 (1.7)	58 (33.5)		
Seizures								
Yes	11 (6.4)	10 (5.8)	0.666*	1.22 (0.490–3.047)	8 (4.6)	13 (7.5)	0.155*	1.983 (0.762–5.162)
No	72 (41.6)	80 (46.2)			36 (20.8)	116 (67.1)		
Focal neurological deficits								
Yes	59 (34.1)	64 (37)	0.997*	0.99 (0.517–1.928)	36 (20.8)	87 (50.3)	0.069*	2.17 (0.92–5.08)
No	24 (13.9)	26 (15)			8 (4.6)	42 (24.3)		
Visual disturbance								
Yes	49 (28.3)	53 (30.6)	1.00*	1.01 (0.549–1.845)	27 (15.6)	75 (43.4)	0.727*	1.14 (0.568–2.304)
No	34 (19.7)	37 (21.4)			17 (9.8)	54 (31.2)		
Motor disturbance								
Yes	10 (5.8)	10 (5.8)	1.00*	1.09 (0.431–2.784)	6 (3.5)	14 (8.1)	0.594*	1.297 (0.466–3.612)
No	73 (42.2)	80 (46.2)			38 (22)	115 (66.5)		
Sensory disturbance								
Yes	1 (0.6)	2 (1.2)	1.00*	0.54 (0.048-6.030)	1 (0.6)	2 (1.2)	1.00*	1.47 (0.131–16.694)
No	82 (47.4)	88 (50.9)			43 (24.9)	127 (73.4)		
Cranial nerve palsy								
Yes	22 (12.7)	14 (8.1)	0.092*	1.95 (0.925–4.145)	14 (8.1)	22 (12.7)	0.052*	2.27 (1.037–4.966)
No	61 (35.3)	76 (43.9)			30 (17.3)	107 (61.8)		
Tumor location								
Convexity	23 (13.3)	25 (14.5)	0.564*	0.99 (0.512–1.940)	23 (13.3)	25 (14.5)	1.00*	0.99 (0.512–1.940)
Base	60 (34.7)	65 (37.6)			60 (34.7)	65 (37.6)		
Meningioma grade								
Grade I	77 (44.5%)	86 (49.7)	0.323*	0.597 (0.162–2.195)	40 (23.1)	123 (71.1)	0.229*	0.488 (0.131–1.816)
Grade II–III	6 (3.5)	4 (2.3)			4 (2.3)	6 (3.5)		

NLR = neutrophile-lymphocyte ratio; MLR = monocyte-lymphocyte ratio; OR = odds ratio
*Chi Square

significantly associated with higher NLR and MLR values. Hyperostosis and edema were not significantly associated with NLR and MLR values either.

Based on **Table 3**, in the analysis of peritumoral edema in relation to clinical and tumor characteristics, it was found that edema is associated with the occurrence of seizures and tumor recurrence, with an odds ratio (OR) of 11.6 (95% CI: 2.59–52.18). Other clinical features were not significantly associated with the presence of edema. Additionally, the tumor size had a larger median volume in subjects with edema, 378.77 cm^3 (range: 1.21–10,095) compared to those without edema, which had a median volume of 94.75 cm^3 (range: 2.88–910.38). Similarly, the NLR was higher in subjects with edema, with a median of 2.50 (range: 0.72–9.73) compared to those without edema, with a median of 2.11 (range: 0.93–7.33).

Tumor size and peritumoral edema index were measured in 126 subjects. From **Table 4**, it can be seen that subjects with seizures had a higher median edema index of 1.59 (range: 0–7.98) compared to those without seizures, who had a median of 0 (range: 0–28.2). Tumor size did not show a significant difference in median values between subjects with and without seizures. Higher median edema indices and larger tumor sizes were observed in subjects with motor impairment, tumors located in the convexity, and higher tumor grades ($p < 0.001$). Grade II–III meningiomas had significantly higher median edema indices and tumor sizes ($p < 0.001$).

In the recurrence analysis, several factors were found to be significant in bivariate analysis ($p < 0.05$), including edema, Simpson grade, NLR, and MLR. Tumor size also showed significance with a p-value of 0.054. Based on the bivariate analysis, five factors with $p < 0.2$ were included in the multivariate analysis using the backward enter method. The multivariate analysis revealed that MLR was the significant factor influencing recurrence, with an adjusted odds ratio (aOR) of 12.647 (95% CI: 2.355–67.919) (**Table 5**).

DISCUSSION

The findings of this study align with previous research, such as that by Kuranari et al. [8] and Qin [9], highlighting the utility of inflammatory markers like NLR and MLR in predicting meningioma recurrence. While variations in cut-off values and diagnostic performance exist across studies, these differences could be attributed to variations in patient demographics, study design, and methodology. The higher AUC and cut-off values found in this study may suggest a more effective diagnostic tool within this

Table 3. The relationship between edema and clinical presentation, grade, tumor characteristics, recurrence, tumor size, and inflammatory markers (n = 153)

	Edema		P	OR (CI 95%)
	Yes (%)	No (%)		
Headache				
Yes	53 (34.6)	46 (30.1)	0.196*	1.55 (0.79–3.03)
No	23 (15.0)	31 (20.3)		
Seizure				
Yes	18 (11.8)	2 (1.3)	**< 0.001***	11.6 (2.59–52.18)
No	58 (37.9)	75 (49)		
Focal neurological deficits				
Yes	56 (36.6)	55 (35.9)	0.755*	1.12 (0.55–2.28)
No	20 (13.1)	22 (14.4)		
Tumor location				
Convexity	32 (20.9)	11 (7.2)	0.000*	4.36 (1.99–9.56)
Base	44 (28.8)	66 (43.1)		
Tumor size	378.77 (1.21–10.095)	94.75 (2.88–910.38)	< 0.001**	
NLR	2.50 (0.72–9.73)	2.11 (0.93–7.33)	0.012**	
MLR	0.24 (0.12–0.94)	0.22 (0.11–0.56)	0.205**	

NLR = neutrophile-lymphocyte ratio; MLR = monocyte-lymphocyte ratio; CI = confidence interval; OR = odds ratio
*Chi Square
**Mann-Whitney

Table 4. The relationship between edema index and tumor size with clinical and tumor characteristics of subjects (n = 126)

	Edema Index		Tumor size	
	Median (min-max)	P	Median (min-max)	P
Headache				
Yes	0.94 (0–28)	0.226*	194.44 (1.21–10.095)	0.129*
No	0 (0–5.09)		174.68 (2.88–1.071)	
Seizures				
Yes	1.59 (0–7.98)	**0.0018**	246.92 (22.6–1150)	0.209*
No	0 (0–28.02)		177.66 (1.21–10.095)	
Focal neurological deficits				
Yes	0.08 (0–28)	0.946*	199.01 (1.21–10.095)	0.026*
No	0.44 (0–6.22)		100.69 (4.07–1.150)	
Visual disturbance				
Yes	0 (0–28.02)	0.022*	184.18 (1.21–10.095)	0.638*
No	1.18 (0–7.98)		206.75 (4.07–1.849)	
Motor disturbance				
Yes	1.91 (0.3–7.98)	**< 0.001***	723.59 (127–1.245)	**< 0.001***
No	0 (0–28.02)		146.45 (1.21–10.095)	
Sensory disturbance				
Yes	1.33 (1.33–4.28)	0.092*	272.15 (199.3–1.071)	0.216*
No	0 (0–28.02)		190.7 (1.21–10.095)	
Cranial nerve palsy				
Yes	0.6 (0–10.63)	0.864*	199.01 (1.21–3.895)	0.437*
No	0 (0–28.02)		184.18 (2.88–10.095)	
Tumor location				
Convexity	1.63 (0–28.02)	**< 0.001***	441.25 (10.75–10.095)	**< 0.001***
Base	0 (0–10.63)		124.55 (1.21–1.849)	
Meningioma grade				
Grade I	0 (0–28.02)	**< 0.001***	177.66 (1.21–3.893)	**< 0.001***
Grade II–III	0.3 (0–4.28)		910.38 (50.24–10.095)	

** Mann-Whitney

Table 5. Factors influencing recurrence

	Bivariate		Multivariate	
	P	OR (CI 95%)	p	aOR (CI 95%)
Tumor location	0.317	1.96 (0.591–6.505)		
Meningioma grade	0.478	0.93 (0.887–0.967)		
Peritumoral edema	**0.031**	**5.03 (1.05–24.14)**	0.052	8.865 (0.981–80.114)
Tumor size	**0.054**	**4.509 (0.918–22.144)**		
NLR	**0.002**	**13.59(1.715–107.815)**		
MLR	**< 0.001**	**10.8 (2.774–42.047)**	**0.003**	**12.647 (2.355–67.919)**
Simpson grade	**0.031**	**0.267 (0.077–0.925)**	0.076	3.920 (0.866–17.739)

NLR = neutrophile-lymphocyte ratio; MLR = monocyte-lymphocyte ratio; CI = confidence interval; OR = odds ratio; aOR = adjusted odds ratio

specific population, underscoring the importance of context when applying predictive markers in clinical practice. Furthermore, the stronger performance of MLR in this study compared to others highlights its potential as a valuable marker, particularly in settings where a more accurate prediction of recurrence is essential. Future research could benefit from exploring how these markers interact with other clinical variables to enhance predictive accuracy across diverse patient populations [8,9].

In acute inflammation, there is an increase in systemic neutrophil levels. As inflammation becomes chronic, lymphocyte levels decrease, and resident macrophages require assistance from peripheral monocytes in the inflamed area. Meningiomas, being slow-growing brain tumors located outside the blood-brain barrier, are conducive to a pattern of chronic peripheral inflammation [10].

These cut-off values will be used as a basis for grouping subjects for further analysis related to clinical symptoms, peritumoral edema, and meningioma recurrence. Subjects will be divided into two groups based on NLR < 2.415 and ≥ 2.415, and similarly for MLR, into groups with MLR < 0.295 and ≥ 0.295.

Headache was the only clinical symptom significantly associated with both NLR and MLR in this study. Subjects with headaches had significantly higher NLR and MLR values. Although no previous studies have directly linked clinical symptoms with peripheral inflammatory markers in meningioma, this finding is consistent with evidence that higher levels of prostaglandin E2 (PGE2) are present in meningioma patients with headaches [11]. The presence of prostaglandin is associated with neutrophil activation, migrating to the inflamed area [12].

Among all clinical symptoms, seizures were significantly associated with peritumoral edema and the edema index. Subjects with seizures had significantly more pronounced peritumoral edema compared to those without seizures. The association between seizures and peritumoral edema in meningiomas has been well-documented, as peritumoral edema fluid contains high levels of glutamate and aspartate, which can propagate seizures [13]. Peritumoral edema also indicates meningioma invasion into the brain parenchyma [14]. This finding aligns with Morsy et al. [15], who identified peritumoral edema as a predictive factor for seizures in meningiomas. Similarly, Lieu et al. found an association between seizures, peritumoral edema, and the location of meningiomas in the convexity [13].

Although edema was not associated with focal neurological deficits in this study, subjects with motor impairments (hemiparesis or hemiplegia) had higher median tumor size and edema index values. This is because the median edema index and tumor size were larger in the convexity area compared to the base. Lesions in this area are more likely to exert pressure on the motor cortex, consistent with the theory of focal deficits in meningiomas. Edema causes cortical distortion and perfusion disturbances, leading to clinical impairments based on the involved area [16,17].

This study also found that edema was associated with median NLR, with subjects exhibiting edema having higher NLR values than those without edema. Inflammatory factors such as IL-6, MMP-9, tenascin, and e-cadherin are associated with peritumoral edema formation through regulation of vascular permeability, modulation of angiogenesis, and invasion into the brain parenchyma. These factors activate peripheral neutrophils to migrate to the tumor area. Kemerdere et al. [19] also reported a significant increase in NLR in meningioma patients with peritumoral edema [18,19].

However, the involvement of mast cells and macrophages in peritumoral edema remains unclear, suggesting that peripheral monocytes might not be involved. This is consistent with the finding in this study that there was no difference in MLR values concerning peritumoral edema.

Subjects with grade II-III meningiomas in this study had a higher median edema index of 0.3 (0–4.28) compared to grade I meningiomas, which had a median index of 0 (0–28.02). More malignant meningiomas induce greater inflammation, vascular factors, and a higher mitotic index, leading to an increased cascade of peripheral inflammatory cells due to cytokines and chemokines secreted by the tumor. Kim et al. [20] similarly found a trend of greater peritumoral edema in grade II–III meningiomas compared to grade I.

The median tumor size in this study was also higher in grade II–III meningiomas, 910.38 cm^3 (range: 50.24–10,095), compared to grade I meningiomas, 177.66 cm^3 (range: 1.21–3,893). The meningioma grade is determined by the tumor's mitotic index, with higher mitosis rates leading to higher grades and faster growth. This finding is consistent with Ressel et al. [21], who reported median tumor sizes of 23.1 ± 30 cm^3 for grade I and 45.3 ± 38.2 cm^3 for grade II–III meningiomas.

This study identified several factors influencing recurrence, including edema, tumor size, Simpson grade, NLR, and MLR. Of these factors, MLR was the most significant predictor of recurrence ($p < 0.001$). Meningioma recurrence is often linked to the tumor microenvironment. Macrophage infiltration, as reported by Proctor et al. [22], plays a role in meningioma progression and recurrence, particularly M2 macrophages. Chronic inflammation continuously activates resident macrophages, leading to the involvement of peripheral monocytes as monocyte-derived macrophages. This explains the increased MLR ratio, especially in subjects with recurrence ($p < 0.001$).

After adjusting for other risk factors, multivariate analysis revealed that only MLR was directly associated with recurrence. A high MLR (≥ 0.295) posed a 13-fold higher risk of recurrence compared to a low MLR. This is likely due to the inflammatory activity in the tumor

microenvironment being closely linked to recurrence. The involvement of macrophages in this process can affect the MLR ratio in meningioma patients [22].

This study is the only one that explores inflammatory markers in relation to clinical symptoms, and it is the first to utilize inflammatory markers in this context. Additionally, it is the first study in Indonesia to investigate clinical symptoms of meningioma in relation to inflammatory markers, edema, and tumor size.

However, there are some limitations. The study was retrospective, so it was hard to know the actual condition of patients when NLR and MLR were measured, which could cause bias. The sample size was enough for correlation analysis but too small for recurrence analysis, so the recurrence results may not represent the wider meningioma patient population. Additionally, NLR and MLR were not compared with the tumor microenvironment to check if the inflammation in the blood matched the inflammation around the tumor.

CONCLUSIONS

This study demonstrates a significant association between higher values of NLR and MLR with clinical symptoms, particularly headache, and with meningioma recurrence. The findings reveal that elevated NLR correlates with peritumoral edema, while MLR presents the strongest predictor of meningioma recurrence, increasing the risk 13-fold in cases with high MLR levels. These results support the utility of NLR and MLR as important peripheral inflammation markers that can help predict clinical symptoms and tumor recurrence in meningioma patients, with MLR serving as the more robust predictor.

DECLARATIONS

Competing interest

The author(s) declare no competing interest in this study.

Ethics approval and consent to participate

The study was conducted and approved by The Ethics Committee of the Faculty of Medicine, University of Indonesia, RSUPN Dr. Cipto Mangunkusumo (Protocol Number: 21-10-1047).

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgment

The Author(s) wish to thank to the leadership and faculty of the Faculty of Medicine, Universitas Indonesia, and to the staff at Dr. Cipto Mangunkusumo Hospital, Jakarta, for providing the facilities and support essential for the completion of this education and research.

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