The Journal of International Advanced Otology

J Int Adv Otol 2025; 21: 1–11 • DOI: 10.5152/iao.2025.241729

Review

Association Between Hematological Indices of Inflammation and Pathogenesis and Prognosis of Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-Analysis

Ranshi Zhao, Ya He, Cheng Zhong

Department of Otolaryngology, Southwest Hospital, Army Medical University (First Affiliated Hospital, Third Military Medical University), Chongqing, China

ORCID iDs of the authors: R.Z. 0009-0006-1462-9178, C.Z. 0000-0002-3346-0578.

Cite this article as: Zhao R, He Y, Zhong C. Association between hematological indices of inflammation and pathogenesis and prognosis of sudden sensorineural hearing loss: A systematic review and meta-analysis. *J Int Adv Otol.* 2025, 21(4), 1729, doi: 10.5152/iao.2025.241729.

Chronic inflammation has been proposed as a contributing factor in the pathogenesis of sudden sensorineural hearing loss (SSNHL). The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) are well-established indices of inflammation, but their roles in SSNHL pathogenesis and prognosis remain controversial. This meta-analysis aimed to explore these associations. A systematic review was performed by 2 independent investigators across PubMed, Web of Science, Cochrane Library, and Embase databases. The quality of included studies was assessed using the Newcastle-Ottawa Scale. Twenty-six studies including 2392 SSNHL patients and 1865 controls were included. Recovery data were available for 1343 patients, of whom 785 recovered and 558 did not. Meta-analysis revealed that both NLR (standardized mean difference [SMD] = 1.082, 95% CI = 0.949, 1.216, $P < .001$) and PLR (SMD = 0.516, 95% CI = 0.333, 0.700, $P < .001$) were significantly elevated in SSNHL patients compared to controls. MPV (SMD = 1.103, 95% CI = 0.820, 1.483, $P = .516$) showed no significant difference. Additionally, higher NLR (SMD = −0.472, 95% CI = −0.784, −0.160, $P = .003$) and PLR (SMD = −0.327, 95% CI = −0.630, −0.023, $P = .035$) were associated with non-recovery in SSNHL, whereas differences in MPV (SMD = −0.352, 95% CI = −0.881, 0.177, $P = .192$) were not statistically significant. NLR and PLR may be involved in the pathogenesis of SSNHL and may serve as cost-effective and accessible prognostic markers.

KEYWORDS: Sudden sensorineural hearing loss, hematologic markers, pathogenesis, meta-analysis, prognosis

INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is defined by an acute onset of hearing impairment of at least 30 dB across 3 consecutive frequencies within a 72-hour period.[1] The pathogenesis of SSNHL is multifactorial, with contributing factors including viral infections, chronic inflammation, immune dysfunction, and vascular microcirculatory disturbances.[2] Recent research has increasingly emphasized the role of chronic inflammation in SSNHL pathogenesis,[3,4] suggesting its involvement in microvascular damage, atherosclerosis,[4] and immune-mediated responses within the cochlea, ultimately increasing the risk of cochlear ischemia.[5]

Hematologic indices, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV), have been investigated as potential biomarkers for SSNHL. Mean platelet volume reflects platelet activation, which may be associated with thrombotic events and hypercoagulability,[6] while NLR and PLR have been proposed as prognostic indicators for SSNHL.[5] These indices are regarded as more stable markers of systemic inflammation compared to cytokines such as interleukin-6 (IL-6), IL-1β, and IL-8.[7] However, the utility of these markers remains debated, with some studies challenging their relevance.[8,9] Given the conflicting evidence, a meta-analysis was conducted to clarify the association between these hematologic markers and both the pathogenesis and prognosis of SSNHL.

Corresponding author: Cheng Zhong, e-mail: agm95zc@tmmu.edu.cn
Received: November 19, 2024 • **Revision Requested:** February 23, 2025 • **Last Revision Received:** March 16, 2025 • **Accepted:** April 5, 2025 • **Publication Date:** July 9, 2025
Available online at www.advancedotology.org

METHODS

A comprehensive literature search was conducted across PubMed, Cochrane Library, Web of Science, and Embase databases from their inception to January 31, 2023. The search strategy combined Medical Subject Headings and free-text terms, including "Hearing Loss," "Sudden," "blood cell," "lymphocyte," "neutrophil," "platelet," "leukocyte," "NLR," "neutrophil-to-lymphocyte ratio," "PLR," "platelet-to-lymphocyte ratio," "mean platelet volume," and "MPV." Additionally, reference lists from all retrieved articles were manually reviewed to identify any further relevant studies. As this study is a retrospective literature review, ethical approval was not required.

Inclusion Criteria: 1. Studies that compare hematological parameters between healthy individuals and SSNHL patients, as well as between those who have recovered and those who have not. 2. Provision of mean values and SDs for the indices. 3. Articles that outline logical treatment modalities, along with recovery and diagnostic benchmarks. 4. Original research that is either retrospective or prospective in nature, with publications exclusively in English. 5. For multiple studies concerning the same cohort, only the most representative study was selected.

Exclusion Criteria: 1. Types of studies excluded: letters, reviews, abstracts from conferences, and case reports. 2. Research lacking adequate basic patient data or not available in English. 3. Instances of duplicate publication. 4. Studies where hematologic indices could be influenced by factors such as prior steroid therapy, infectious diseases (acute or chronic), or rheumatologic, hematologic, and endocrine disorders.

Two independent reviewers assessed the titles and abstracts to identify studies evaluating hematologic markers related to the pathogenesis or prognosis of SSNHL. Studies meeting the inclusion criteria underwent full-text review. Hematologic indices were reported as mean ± SD. Quality assessment was performed independently, with discrepancies resolved through consensus. Extracted data included the first author's name, publication year, study region, study design, sample size, demographic data (age, sex), baseline matching, NLR, PLR, MPV values, follow-up duration, type of steroid administered, and patient recovery criteria. Study quality was evaluated using the Newcastle-Ottawa Scale, with scores ranging from 0 to 9.[10]

MAIN POINTS

- Elevated neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) may be associated with sudden sensorineural hearing loss (SSNHL), suggesting that inflammation may play a role in SSNHL pathogenesis.
- No significant differences were observed in mean platelet volume when comparing SSNHL patients with controls, nor between recovered and unrecovered groups, indicating limited evidence for its use as an inflammatory marker in SSNHL.
- Higher levels of NLR and PLR were associated with poorer recovery outcomes in SSNHL patients, supporting their potential prognostic relevance.

Statistical Analysis

All statistical analyses were performed using Stata 15.0 software (StataCorp; Texas; USA). The standardized mean difference (SMD) and 95% CIs were calculated, with a significance level of $P < .05$. Heterogeneity among the included studies was assessed using the Q-test and the I^2 statistic ($P > .1$ indicating no significant heterogeneity; $I^2 > 50\%$ indicating substantial heterogeneity).[11] A random-effects model was employed for substantial heterogeneity, while a fixed-effects model was used otherwise. Subgroup analyses were conducted based on literature type, geographic region, age, sample size, steroid type, follow-up duration, audiometric device brand, and recovery criteria to identify potential confounders. Sensitivity analyses were performed by sequentially excluding each study to evaluate the robustness of the results. Publication bias was assessed using Egger's test,[12] with $P > .05$ indicating no significant bias. In the presence of publication bias, the trim-and-fill method was applied to validate the meta-analysis results.[13]

RESULTS

Literature Search and Research Characteristics

The initial search identified 598 articles, with an additional study found through reference list examination of the included papers. After removing duplicates (n = 432), 166 articles remained from the primary search. Title and abstract screening led to the exclusion of 121 articles. From the remaining 41 articles, several were excluded for the following reasons: 1 lacked essential demographic data such as age and sex; 2 focused on different hematologic outcomes related to inflammation; 5 did not report mean and SD values for NLR, PLR, or MPV; 2 were based on the same cohort; and 6 were letters to the editor. Ultimately, 26 studies[3,6-9,14-34] were included in the meta-analysis, encompassing 2392 patients with SSNHL and 1865 healthy controls (Figure 1). The studies by Sun[15,27] and Karakurt[23] included 4 distinct groups, while Li's study[32] comprised 2, culminating in 36 separate group analyses. A total of 24 studies[3,6-9,14,15,18-34] examined variations in hematologic parameters between patients with SSNHL and healthy controls, encompassing 2209 SSNHL patients and 1865 healthy individuals. Additionally, 13 studies[3,7,9,15-17,19,20,24,25,27,28,34] investigated the differences in hematologic indicators between patients who recovered and those who did not, including 1343 individuals, with 785 recovered and 558 non-recovered. The key characteristics of the included studies are summarized in Tables 1 and 2.

Neutrophil-to-Lymphocyte Ratio in Sudden Sensorineural Hearing Loss and Control Groups

Fifteen studies[3,9,19-23,25-32] encompassing 25 cohorts, evaluated the association between the NLR and SSNHL, involving 1535 patients with SSNHL and 1298 healthy controls. Given the significant heterogeneity among the included studies ($P < .001$, $I^2 = 60.9\%$), a random-effects model was utilized to pool the results. The analysis demonstrated that NLR levels were significantly elevated in the SSNHL group compared to the control group (SMD = 1.082, 95% CI = 0.949, 1.216, $P < .001$; Figure 2A). Subgroup analysis identified baseline matching and the interval from SSNHL onset to blood collection as sources of heterogeneity, while region and study design did not contribute to the heterogeneity (Table 3).

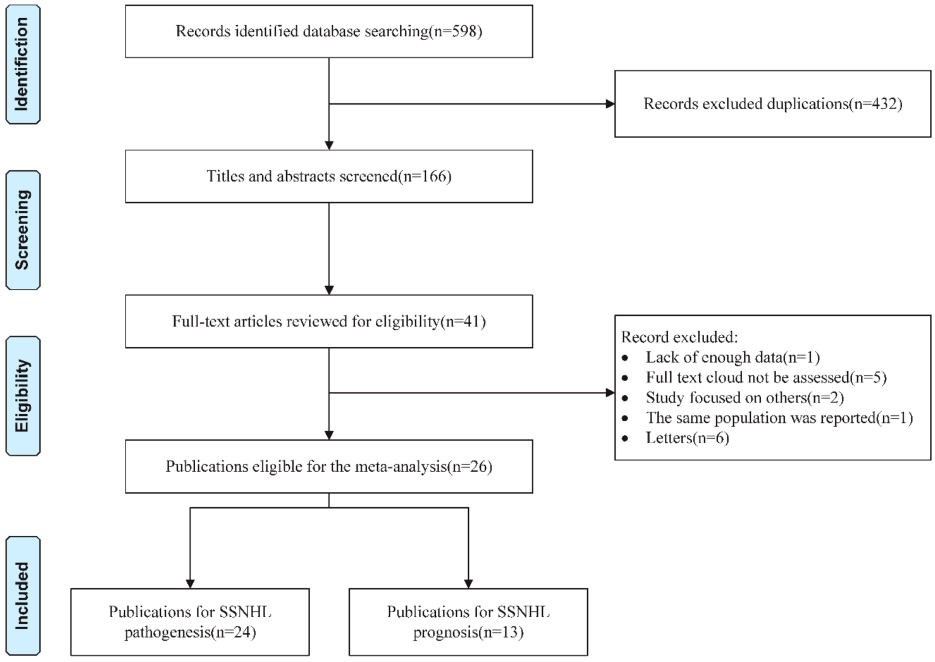

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of the selection process.

Platelet-to-Lymphocyte Ratio in Sudden Sensorineural Hearing Loss and Control Groups

Ten studies[3,9,15,19,20,22,23,26,30,31] across 19 cohorts assessed the association between the PLR and SSNHL, involving 1120 SSNHL patients and 1008 healthy controls. Due to the significant heterogeneity among the studies ($P < .001$, $I^2 = 75.5\%$), random-effects model was applied. The analysis indicated that PLR values were significantly elevated in the SSNHL group compared to the healthy control group (SMD = 0.516, 95% CI = 0.333, 0.700, $P < .001$; Figure 2B). Subgroup analysis identified sample size as a source of heterogeneity (Table 3).

Mean Platelet Volume in Sudden Sensorineural Hearing Loss and Control Groups

Eight studies[6,8,14,15,18,22,25,33] examined the role of MPV in SSNHL pathogenesis, including 568 SSNHL patients and 550 healthy controls. Significant heterogeneity was noted across these studies ($P = .001$, $I^2 = 79.6\%$), prompting the use of a random-effects model. The pooled analysis showed a significant difference in MPV levels between SSNHL patients and controls (SMD = 0.313, 95% CI = 0.042, 0.584, $P = .024$; Figure 2C). Subgroup analysis indicated that the region was a source of heterogeneity (Table 3).

Neutrophil-to-Lymphocyte Ratio for Recovered and Non-recovery Groups

A meta-analysis of 11 studies[3,7,9,16,17,19,20,24,25,27,28] across 14 cohorts, including 685 patients who recovered from SSNHL and 482 who did not, evaluated the association between NLR and SSNHL prognosis. Significant heterogeneity was present ($P < .001$, $I^2 = 81.5\%$), necessitating a random-effects model. The results revealed a significant difference in NLR levels between recovered and non-recovered groups (SMD = −0.472, 95% CI = −0.784, −0.160, $P = .003$; Figure 3A). Subgroup analyses showed that clinical variables such as region, steroid type, audiometric device brand, definition of "recovery," follow-up period, interval from SSNHL onset to blood collection, and hormone treatment did not contribute to heterogeneity (Table 4).

Platelet-To-Lymphocyte Ratio for Recovered and Non-Recovery Groups

Eight studies[3,7,9,15,17,19,27,34] comprising 11 cohorts with a total of 965 patients (569 in the recovery group and 396 in the non-recovery group), were analyzed to evaluate the impact of PLR on SSNHL prognosis. Significant heterogeneity was noted ($P < 0.01$, $I^2 = 75.1\%$), and a random-effects model was applied. PLR levels were significantly higher in the non-recovery group compared to the recovery group (SMD = −0.327, 95% CI = −0.630, −0.023, $P = .035$; Figure 3B). Subgroup analysis indicated that factors such as study design, audiometric device brand, follow-up duration, region, sample size, and steroid type contributed to heterogeneity, whereas the definition of "recovery," interval from SSNHL onset to blood collection, and steroid administration method did not (Table 4).

Mean Platelet Volume for Recovered and Non-Recovery Groups

Five articles[7,15,16,18,25] across 8 cohorts, examined the impact of MPV on SSNHL prognosis, including 266 patients in the recovery group and 198 in the non-recovery group. Due to substantial heterogeneity ($P < .01$, $I^2 = 84.2\%$), a random-effects model was applied. No significant difference in MPV levels was observed between recovered and non-recovered groups (SMD = −0.352, 95% CI = −0.881, 0.177, $P = .192$; Figure 3C). Subgroup analysis identified the definition of "recovery," interval from SSNHL onset to blood collection, steroid type, and method of steroid administration as sources of heterogeneity (Table 4).

Sensitivity Analysis and Publication Bias

A leave-one-out sensitivity analysis was conducted (Figure 4), with no significant changes observed in the overall results, confirming the robustness of the meta-analysis. Publication bias was detected in studies evaluating MPV in SSNHL pathogenesis, while no bias was observed in NLR and PLR studies (Egger's test: NLR, $P = .968$; PLR, $P = .216$; MPV, $P = .037$). This was further supported by the funnel plot shape. For SSNHL prognosis, no publication bias was identified for

Table 1. Main Characteristics of the Included Studies in the Meta-Analysis of the Association of Neutrophil-To-Lymphocyte Ratio, Platelet-To-Lymphocyte Ratio and Mean Platelet Volume in Sudden Sensorineural Hearing Loss Pathogenesis

Study	Study Design	Region	Duration Time	Baseline Matching	Simple Size (case/control)	Time Intervals Elapsed from the Onset of SSNHL to Blood Sampling	NOS
Durmuş K. (2016)	RC	Türkiye	2008-2014	Age, gender	140/132	Within 7 days	9
Öçal R. (2020)	RC	Türkiye	2016-2017	Age, gender	40/45	Within 3 days	7
Kum RO. (2015)	RC	Türkiye	2010-2013	Age, gender	59/59	Within 7 days	7
Sancaktar ME. (2020)	RC	Türkiye	2016-2018	Age, gender	68/30	Within 3 days	8
Sun Y. (2018)	RC	China	NR	Age, gender	40/31	Within 7 days	8
					33/31		
					36/31		
					34/31		
Ulu S.(2013A)	RC	Türkiye	2007-2013	Age, gender	47/45	NR	7
Seo YJ.(2014)	RC	Korea	2009-2013	Age, gender	348/537	Within 7 days	8
Özler GS.(2014)	RC	Türkiye	NR	Age	40/40	NR	7
Yao Y.(2023)	RC	China	2019-2021	NR	29/75	NR	7
					27/75		
					31/75		
					23/75		
Çiçek T.(2021)	RC	Türkiye	NR	NR	60/30	NR	6
Qiao XF.(2019)	RC	China	2015-2016	Age, gender	60/60	NR	7
Li H.(2015)	RC	China	2007-2013	NR	86/14	NR	7
					45/14		
Mirvakili A.(2016)	PC	Iran	2013-2015	Age, gender, BMI	108/108	NR	7
Cayir S.(2021)	PC	Türkiye	NR	Age, gender	47/41	Within 5 days	8
Sun Y.(2017)	PC	China	NR	Age, gender	37/31	Within 7 days	8
					28/31		
					32/31		
					32/31		
Ulu S. (2013B)	RC	Türkiye	2007-2012	Age, gender	40/40	NR	7
Koçak HE. (2017)	RC	Türkiye	2014-2015	NR	45/47	Within 7 days	6
Karli R. (2013)	RC	Türkiye	2006-2011	Age, gender	46/46	NR	7
Sagit M. (2013)	RC	Türkiye	NR	Age, gender	31/31	NR	8
İkinciogullari A. (2015)	RC	Türkiye	2005-2013	Age, gender	102/119	NR	7
Guo Y. (2021)	PC	China	2018-2019	NR	169/132	other	6
Ezerarslan H. (2016)	PC	Türkiye	NR	Age, gender	62/49	NR	8
Karakurt SE. (2022)	RC	Türkiye	2014-2020	Age, gender	23/30	NR	7
					48/30		
					26/30		
					39/30		
Koçak HE. (2016)	RC	Türkiye	2008-2016	Age, gender	93/93	NR	7

BMI, body mass index; NOS, Newcastle-Ottawa scale; NR, none reported; PC, prospective case-control; RC, retrospective case-control; SSNHL, sudden sensorineural hearing loss.

any of the 3 indicators (Egger's test: NLR, $P = .790$; PLR, $P = .524$; MPV, $P = .285$). The funnel plot showed no discernible asymmetry. In studies assessing MPV's role in SSNHL pathogenesis, publication bias was detected. The trim-and-fill method estimated a deficit of 3 studies. Accordingly, 3 imputed studies were added using Stata 15.0, and a subsequent meta-analysis was conducted. Due to considerable heterogeneity ($P < .001$), a random-effects model was employed. The pooled effect size revealed no significant difference in MPV levels between SSNHL patients and controls (SMD = 1.103, 95% CI = 0.820, 1.483, $P = .516$).

DISCUSSION

The pathogenesis of SSNHL remains unclear.[35] However, several possible contributing factors have been proposed, including viral

Table 2. Main Characteristics of the Included Studies in the Meta-Analysis of the Association of Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio and Mean Platelet Volume in Sudden Sensorineural Hearing Loss Prognosis

Study	Study Design	Region	Recovered/Unrecovered	Definition of "Covered"	Time Intervals Elapsed from the Onset of SSNHL to Blood Sampling	Type of Steroid	Medication Administration	Follow-Up Period	Hearing Instruments	NOS
Durmuş K. (2016)	RC	Türkiye	83/57	≥15 dB HL	≤1 week	Metilprednisolon	Intravenous	1 month	AC40	7
Öçal R. (2020)	RC	Türkiye	27/13	≥15 dB HL	≤1 week	Methylprednisolone	Intravenous	>1 month	AC40	8
Kum RO. (2015)	RC	Türkiye	28/31	≥10 dB HL	≤1 week	Prednisone	Oral	1 month	AC40	8
Sun Y. (2018)	RC	China	34/6	≥15 dB HL	≤1 week	Dexamethasone	Intravenous	1 month	NR	8
			11/22							
			18/18							
			10/24							
Ulu S.(2013A)	RC	Türkiye	21/26	≥10 dB HL	NR	Prednisone	Oral	1 month	AC40	7
Seo YJ. (2014)	RC	Korea	210/138	≥15 dB HL	≤1 week	Prednisone	Intravenous	>1 month	NR	9
Qiao XF. (2019)	RC	China	48/12	≥15 dB HL	NR	Dexamethasone	Intravenous	<1 month	NR	7
Cayir S.(2021)	PC	Türkiye	33/14	≥15 dB HL	≤1 week	Prednisone	Oral	>1 month	AC40	8
Sun Y. (2017)	PC	China	31/6	≥15 dB HL	≤1 week	Dexamethasone	intravenous	1 month	NR	8
			10/18							
			16/16							
			10/22							
Nonoyama H. (2016)	RC	Japan	67/22	≥15 dB HL	NR	Hydrocortisone sodium succinate	Intravenous	>1 month	other	8
Quaranta N. (2015)	RC	Italy	39/55	≥15 dB HL	NR	Prednisone	Oral	1 month	NR	8
Koçak HE. (2017)	RC	Türkiye	27/18	≥15 dB HL	≤1 week	Methylprednisolone	Oral	>1 month	NR	8

NOS, Newcastle-Ottawa scale; NR, none reported; PC, prospective case-control; RC, retrospective case-control; SSNHL, sudden sensorineural hearing loss.

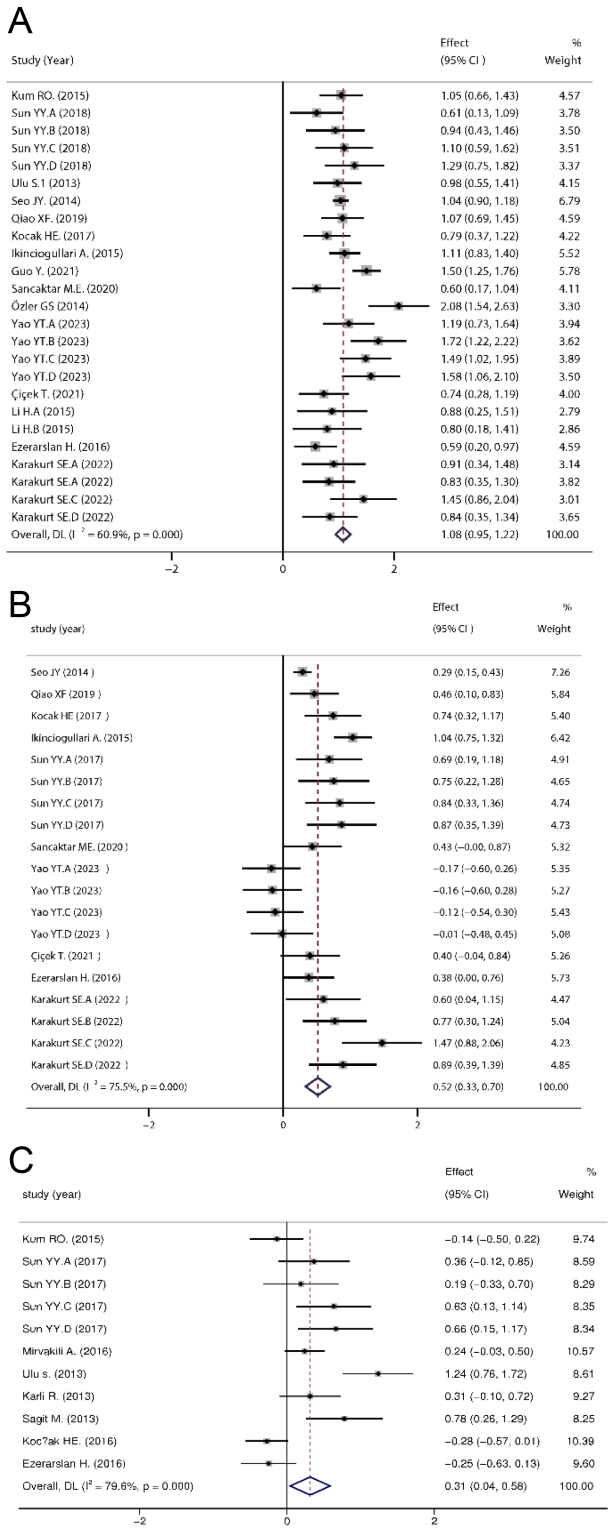

Figure 2. A-C. Forest plot of differences in neutrophil-to-lymphocyte ratio (NLR) levels between patients with SSNHL and healthy controls (A), differences in platelet-to-lymphocyte ratio (PLR) levels between patients with SSNHL and healthy controls (B), and differences in mean platelet volume (MPV) levels between patients with SSNHL and healthy controls (C). SSNHL, sudden sensorineural hearing loss.

infections, chronic inflammation, immune dysregulation, and microvascular disturbances.[5,36] Chronic inflammation, potentially caused by viral or bacterial infections, may lead to vascular insufficiency

Table 3. Subgroup Analyses for the Predictive Value of Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio and Mean Platelet Volume in Sudden Sensorineural Hearing Loss Pathogenesis

Categories		NLR			PLR			MPV		
		No. of Studies	SMD (95% CI)	I^2 (%)	No. of Studies	SMD (95% CI)	I^2 (%)	No. of Studies	SMD (95% CI)	I^2 (%)
Overall		25	1.082 (0.949, 1.216)	60.90	19	0.516 (0.333,0.700)	75.50	11	0.313 (0.042,0.584)	79.60
Study design	RC	22	1.077 (0.939,1.215)	52.60	18	0.525 (0.331,0.720)	76.90	9	0.396 (0.060,0.731)	81.20
	PC	3	1.085 (0.596,1.573)	87.10	1	0.382 (0.004,0.760)	–	2	0.012 (−0.464,0.488)	76.60
Region	Europe	11	0.962 (0.731,1.192)	63.10	9	0.732 (0.512,0.953)	56.30	6	0.252 (−0.205,0.710)	87.70
	Asia	14	1.177 (1.024,1.331)	52.30	10	0.320 (0.098,0.542)	69.30	5	0.460 (0.209,0.711)	0.00
Baseline matching	Age, gender	14	0.955 (0.842,1.068)	12.50	13	0.699 (0.496,0.902)	71.50	10	0.327 (0.011,0.643)	81.60
	NR	9	1.207 (0.951,1.462)	64.50	6	0.114 (−0.193,0.421)	66.30	–	–	–
	other	2	1.568 (0.617,2.518)	89.50	–	–	–	1	0.237 (−0.030,0.505)	
Interval from SSNHL onset to blood collection	Within 7 days	7	1.007 (0.893,1.122)	0	6	0.647 (0.376,0.917)	64.00	5	0.315 (−0.008,0.637)	57.80
	other	2	1.072 (0.190,1.954)	91.70	1	0.434 (−0.000,0.868)	–	–	–	–
	NR	16	1.130 (0.940,1.321)	62.00	12	0.452 (0.164,0.739)	81.50	6	0.313 (−0.109,0.734)	87.20
Sample size	≥100	9	1.176 (0.983,1.369)	68.30	7	0.269 (−0.036,0.574)	84.80	4	−0.095 (−0.356,0.167)	62.80
	<100	16	1.012 (0.824,1.200)	54.50	12	0.681 (0.490,0.872)	44.90	7	0.591 (0.325,0.857)	52.30

MPV, mean platelet volumes; NLR, neutrophil-to-lymphocyte ratio; NR, none reported; PC, prospective case-control; PLR, platelet-to-lymphocyte ratio; RC, retrospective case-control; SMD, standard mean deviation; SSNHL, sudden sensorineural hearing loss.

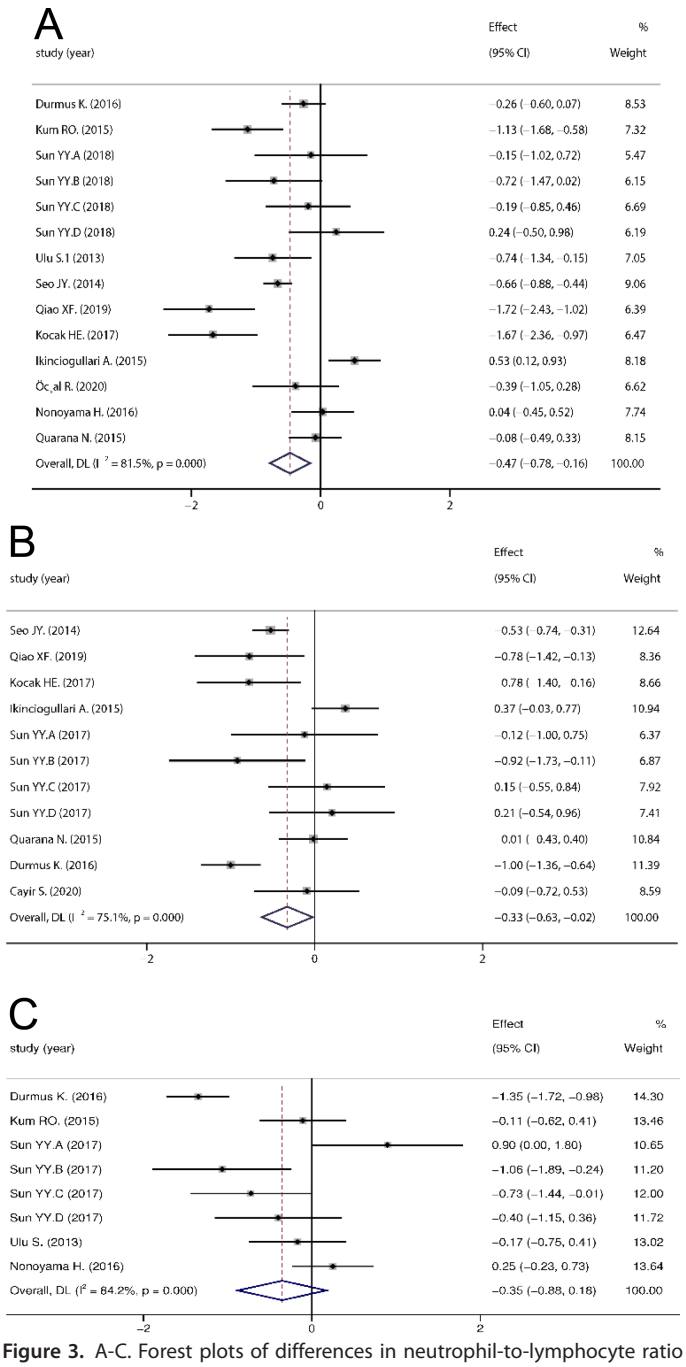

Figure 3. A-C. Forest plots of differences in neutrophil-to-lymphocyte ratio (NLR) levels between the recovered and unrecovered groups (A), differences in platelet-to-lymphocyte ratio (PLR) levels between the recovered and unrecovered groups (B), and differences in mean platelet volume (MPV) levels between the recovered and unrecovered groups (C). SSNHL, sudden sensorineural hearing loss.

through mechanisms such as hemagglutination,[37] capillary edema, and hypercoagulability.[38] These pathophysiological changes increase the risk of microvascular damage and ischemia, particularly affecting cochlear hair cells, which are highly sensitive to changes in blood flow due to their reliance on the labyrinthine artery. As a result, inflammatory processes in the bloodstream may have a detrimental impact on the cochlear vascular system.[36]

Inflammatory markers are commonly recognized as prognostic indicators and have been linked to the severity of inflammation in conditions such as cardiovascular and cerebrovascular diseases, diabetes, and hypertension.[2,37,39] Notably, the NLR and PLR have emerged as composite indicators of inflammation receiving particular attention.[2,39] These ratios are considered more stable than individual markers and are less influenced by systemic factors such as exercise or dehydration.[40] They are easy to measure and provide a cost-effective alternative to other inflammatory biomarkers.[41,42] Mean platelet volume, a widely used parameter, indicates platelet size, function, and activity. Larger platelets are more enzymatically and metabolically active and may promote thrombus formation or hypercoagulability, potentially contributing to the pathogenesis of SSNHL.[7,43]

In the meta-analysis, which included 24 studies across 34 cohorts with a total of 2209 SSNHL patients and 1865 healthy controls, it was observed that both NLR and PLR levels were significantly higher in SSNHL patients compared to healthy controls. However, no statistically significant difference was observed in MPV levels between the 2 groups. These results indicate that NLR and PLR may function as potential markers for the pathogenesis of SSNHL. Further analysis of recovery outcomes, which included 13 studies and 19 cohorts, showed that non-recovered patients had significantly higher NLR and PLR levels than those who recovered, while MPV was not different between the 2 groups. Although the heterogeneity observed could not be attributed to any single subgroup, the robustness of the results was confirmed through sensitivity analysis. These findings could assist clinicians in customizing treatment strategies and prognostic evaluations based on NLR and PLR levels.

Platelets play a role in both thrombosis and inflammation.[44,45] However, within the SSNHL context, NLR has been identified as a more reliable marker for predicting both the onset and prognosis of the disease compared to PLR.[21,40] Moreover, the role of MPV in SSNHL remains controversial. While some scholars have posited that MPV contributes to the pathogenesis of SSNHL,[6,18,43] others have found no significant association.[8,46] Given that MPV can be influenced by a range of factors, including nasal septum deviation, depression, and insulin resistance, caution is advised in interpreting these findings.[1,7,18] In this study, there was a publication bias in the inclusion of studies on the pathogenesis of MPV and SSNHL This bias may originate from the underreporting of negative results and the tendency for researchers from non-English-speaking regions to publish in local journals.[13] As a result, high-quality prospective studies are needed to clarify the relationship between MPV and SSNHL.

In the pathogenesis of SSNHL, both the NLR and PLR may be linked to the underlying pathophysiological mechanisms, demonstrating significant prognostic relevance. Current research indicates that NLR can serve as an independent prognostic marker for SSNHL outcomes.[40] Additionally, it has been reported that patients with higher NLR values show a diminished potential for recovery, with a proposed threshold identified at 6.66.[47] In contrast, a lower critical NLR value of 3.42 has also been proposed.[42]

Furthermore, investigations into the relationship between audiometric curves and inflammatory markers have revealed that elevated levels of NLR and PLR are especially pronounced in patients with descending audiometry. This observation hints at a potential connection between increased inflammatory activity and damage to hair cells, which play a critical role in auditory function.[23] However,

Table 4. Subgroup Analyses for the Predictive Value of Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio and Mean Platelet Volume in Sudden Sensorineural Hearing Loss Prognosis

Categories		NLR			PLR			MPV		
		No. of Studies	SMD (95% CI)	I^2 (%)	No. of Studies	SMD (95% CI)	I^2 (%)	No. of Studies	SMD (95% CI)	I^2 (%)
Overall		14	−0.472 (−0.784,−0.160)	81.50	11	−0.327 (−0.630,−0.023)	75.10	8	−0.352 (−0.881,0.177)	84.20
Study design	RC	–	–	–	6	−0.439 (−0.850,−0.028)	84.30	–	–	–
	PC	–	–	–	5	−0.128 (−0.499,0.244)	20.50	–	–	–
Definition of "recovery"	Siegel criteria	11	−0.486 (−0.800,−0.173)	75.60	10	−0.421 (−0.696,−0.147)	63.40	6	−0.421 (−1.136,0.293)	87.40
	Non-Siegel criteria	3	−0.432 (−1.509,0.644)	92.40	1	0.366 (−0.035,0.766)	–	2	−0.134 (−0.517,0.248)	0.00
Interval from SSNHL onset to blood collection	≤1 week	9	−0.562 (−0.874,−0.251)	67.60	8	−0.448 (−0.756,−0.140)	61.70	6	−0.495 (−1.129,0.140)	83.50
	NR	5	−0.354 (−1.006, 0.299)	88.30	3	−0.091 (−0.660,0.479)	77.00	2	0.071 (−0.337,0.479)	16.80
Brand audiometry device	AC40	5	−0.376 (−0.938,0.187)	85.00	3	−0.251 (−1.171,0.670)	92.20	3	−0.560 (−1.437,0.317)	89.90
	NR	8	−0.614 (−1.037,−0.191)	78.70	8	−0.360 (−0.641,−0.079)	50.90	4	−0.345 (−1.117,0.427)	73.50
	other	1	0.035 (−0.446,0.517)	–	–	–	–	1	0.251 (−0.232,0.734)	–
Follow-up period	1 month	9	−0.266 (−0.617,0.086)	73.50	7	−0.191 (−0.676,0.293)	81.60	7	−0.449 (−1.001,0.103)	82.00
	>1 month	4	−0.637 (−1.197,−0.077)	81.80	3	−0.499 (−0.763,−0.235)	19.30	1	0.251 (−0.232,0.734)	–
	<1 month	1	−1.724 (−2.430,−1.018)	–	1	−0.776 (−1.424,−0.128)	–	–	–	–
Medication administration	Intravenous	9	−0.423 (−0.738,−0.108)	69.30	7	−0.492 (−0.824,−0.161)	62.70	6	−0.421 (−1.136,0.293)	87.40
	Oral	5	−0.588 (−1.335,0.160)	90.70	4	−0.089 (−0.531,0.354)	68.20	2	−0.134 (−0.517,0.248)	0.00
Region	Europe	7	−0.497 (−0.994,−0.000)	86.00	5	−0.302 (−0.865,0.262)	86.70	6	−0.421 (−1.136,0.293)	87.40
	Asia	7	−0.458 (−0.882,−0.033)	74.90	6	−0.375 (−0.706,−0.044)	44.70	2	−0.134 (−0.517,0.248)	0.00
Type of steroid	Prednisone	5	−0.401 (−0.940,0.138)	88.80	4	−0.084 (−0.538,0.369)	82.00	2	−0.134 (−0.517,0.248)	73.50
	Dexamethasone	5	−0.517 (−1.201,0.168)	76.70	5	−0.295 (−0.764,0.173)	48.80	4	−0.345 (−1.117,0.427)	0.00
	Other	4	−0.526 (−1.138,0.085)	81.90	2	−0.947 (−1.256,−0.637)	0.00	2	−0.556 (−2.124,1.011)	96.20
Sample size	≥60	6	−0.332 (−0.791,0.147)	88.80	5	−0.383 (−0.844,0.079)	87.00	2	−0.556 (−2.124,1.011)	96.20
	<60	8	−0.615 (−1.028,−0.203)	66.10	6	−0.262 (−0.644,0.119)	40.90	6	−0.272 (−0.714,0.171)	59.10

MPV, mean platelet volumes; NLR, neutrophil-to-lymphocyte ratio; NR, none reported; PC, prospective case-control; PLR, platelet-to-lymphocyte ratio; RC, retrospective case-control; SMD, standard mean deviation; SSNHL, sudden sensorineural hearing loss.

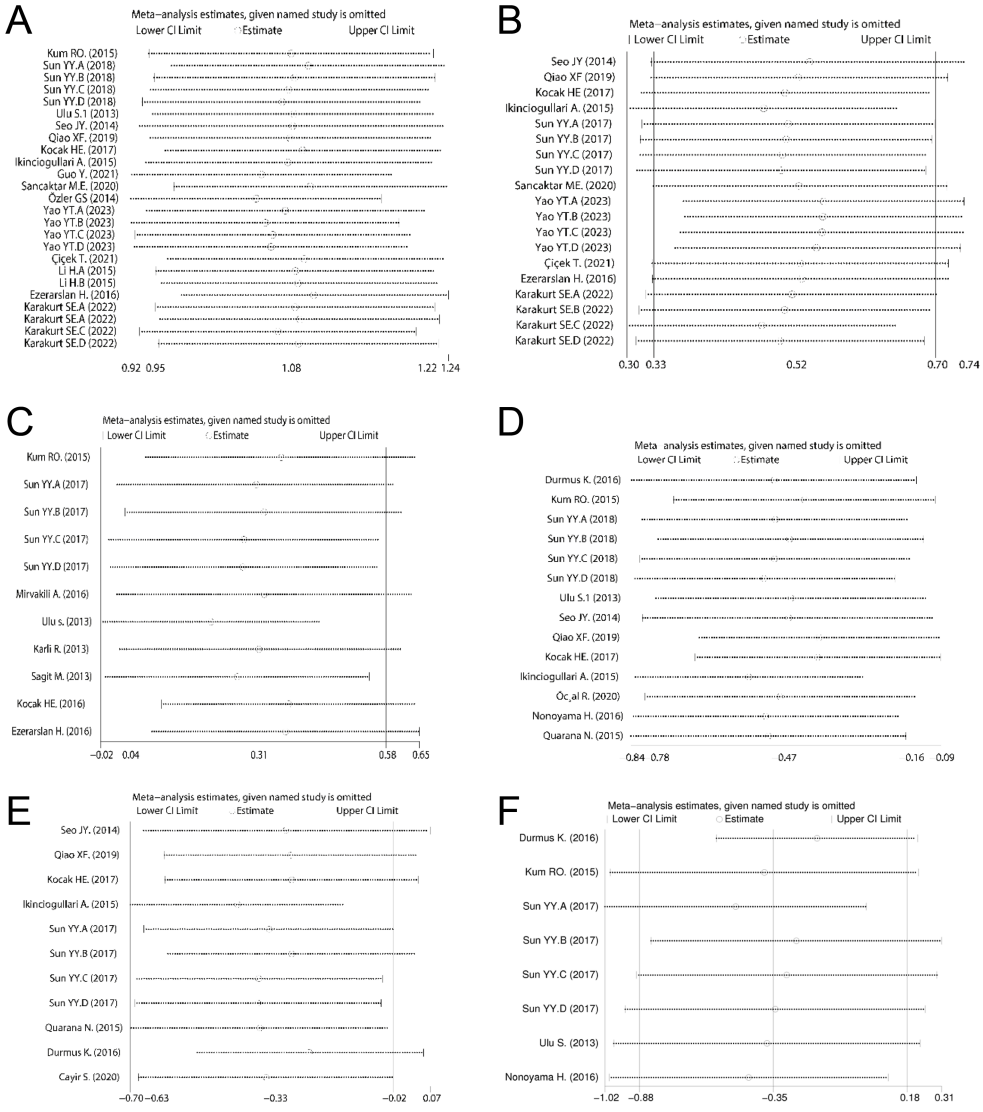

Figure 4. A-F. Effect of individual studies on pooled hazard ratios for the association between NLR, PLR, MPV, and SSNHL. Sensitivity analysis for NLR in the pathogenesis of SSNHL (A). Sensitivity analysis for PLR in the pathogenesis of SSNHL (B). Sensitivity analysis for MPV in the pathogenesis of SSNHL (C). Sensitivity analysis for NLR in the prognosis of SSNHL (D). Sensitivity analysis for PLR in the prognosis of SSNHL (E). Sensitivity analysis for MPV in the prognosis of SSNHL (F). MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

it is noteworthy that some studies have failed to establish a significant correlation between NLR, PLR values, and audiometric curves,[15] suggesting that further exploration is needed to clarify these relationships.

Previous meta-analyses have faced limitations due to narrow focus or a small number of included literatures. For example, 1 study analyzed only 10 papers[2], while another exclusively concentrated on NLR, encompassing just 12 studies.[40] Another meta-analysis included 18 studies but also incorporated research on children and various case reports, potentially limiting the generalizability of its findings.[48] Additionally, some analyses focused on the relationship between SSNHL and platelet-related parameters.[43] In contrast, this meta-analysis builds on previous work by incorporating a larger dataset, with 27 studies involving 2539 SSNHL patients and 1968 healthy controls. By focusing exclusively on adult populations, this study aims to minimize age-related variability. Furthermore, the meta-analysis evaluates the diagnostic and prognostic utility of both NLR and PLR in SSNHL.

This study has several limitations. First, most of the included studies were retrospective in design rather than prospective, and some had relatively small sample sizes, which may introduce selection and information biases. Second, the quality of many of the included studies was suboptimal. Third, variations in the definitions of recovery and differences in inclusion and exclusion criteria among the studies may have contributed to heterogeneity.

CONCLUSION

In summary, the NLR and PLR may play roles in the pathogenesis of SSNHL and could serve as convenient, cost-effective, and routinely available prognostic markers. The relationship between MPV and SSNHL requires further investigation to determine its clinical significance.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – R.Z.; Design – R.Z.; Supervision – C.Z.; Resources – R.Z.; Materials – R.Z., Y.H.; Data Collection and/or Processing – R.Z., Y.H.; Analysis and/or Interpretation – R.Z., C.Z.; Literature Search – R.Z., Y.H.; Writing Manuscript – R.Z., Y.H.; Critical Review – C.Z.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declare that this study received no financial support.

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