e-ISSN: 2722-9807

Sriwijaya Journal of Ophthalmology

[SJO]

https://sriwijayaophthalmology.com

Neutrophil-to-Lymphocyte Ratio as a Predictive Biomarker for Retinopathy of Prematurity: A Systematic Review

Ayu Diah Permatasari[1]*, I Wayan Eka Sutyawan[1], Ni Made Ayu Surasmiati[1]

[1]Department of Ophthalmology, Faculty of Medicine, Universitas Udayana/Prof. Dr. I.G.N.G Ngoerah General Hospital, Denpasar, Indonesia

ARTICLE INFO

Keywords:
Neonatology
Neutrophil-to-lymphocyte ratio
Predictive biomarker
Retinopathy of prematurity
Systemic inflammation

***Corresponding author:**
Ayu Diah Permatasari

E-mail address:
ayudiahpermata@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/sjo.v8i1.130

A B S T R A C T

Introduction: Retinopathy of prematurity (ROP) remains a leading cause of childhood blindness, with its pathogenesis linked to aberrant vascular development and systemic inflammation. There is a critical need for accessible biomarkers to improve risk stratification beyond current screening standards. This systematic review critically appraises the evidence for the neutrophil-to-lymphocyte ratio (NLR), a widely available inflammatory marker, as a predictor of ROP. **Methods:** Following PRISMA 2020 guidelines, a systematic search was conducted in PubMed, ScienceDirect, ProQuest, and SpringerLink for observational studies published between January 1st, 2015, and December 31st, 2024. Studies assessing the association between NLR and ROP in preterm infants were included. Two reviewers independently performed study selection, data extraction, and a formal risk-of-bias assessment using the Newcastle-Ottawa Scale (NOS). A narrative synthesis was performed due to significant heterogeneity. **Results:** The search identified 32 records, with 6 retrospective studies ultimately meeting the inclusion criteria, encompassing a total reported sample of 1,065 infants. The methodological quality of the included studies was low to moderate, with NOS scores ranging from 5 to 7 out of a possible 9. The evidence base was defined by profound methodological heterogeneity, particularly in the timing of blood sample collection, which was unspecified in half of the studies, and inconsistent reporting of core population data. A narrative synthesis of the findings showed that several studies reported a statistical association between an elevated NLR or related inflammatory markers and ROP. However, one study reported no significant association, and the interpretation of others was complicated by a focus on different biomarkers or a lack of statistical significance. **Conclusion:** The available evidence, derived exclusively from retrospective studies of varying quality, suggests a possible association between elevated NLR and ROP, a link supported by strong biological plausibility. However, the current evidence base is severely limited by methodological flaws and profound heterogeneity, making it insufficient to support the adoption of NLR into clinical practice. NLR is not a standalone diagnostic or predictive tool for ROP. Its potential utility can only be realized through large-scale, methodologically rigorous prospective studies designed to overcome the limitations identified in this review.

1. Introduction

Retinopathy of prematurity (ROP) is a vasoproliferative disorder affecting the incompletely vascularized retina of preterm infants and represents a formidable challenge in global pediatric health.[1] It is a leading cause of preventable childhood blindness worldwide. Over the past several decades, monumental advances in perinatal and neonatal medicine have led to a dramatic improvement in the survival rates of increasingly premature and low birth weight infants. This laudable success has, paradoxically, expanded the population of infants at

high risk for developing this potentially devastating condition.[2] Epidemiological data from both developed and developing nations reflect this trend, showing a significant and ongoing burden of ROP. The primary risk factors are well-established and form the basis of all screening programs: low gestational age (GA) and low birth weight (LBW), which together serve as proxies for the degree of retinal vascular immaturity at birth.[3]

The current global standard of care for ROP management is predicated on timely and repetitive screening through binocular indirect ophthalmoscopy.[4] This paradigm, while effective in identifying diseases that have reached a treatment-requiring threshold, is fraught with substantial limitations that underscore an urgent need for innovation. These challenges are a daily clinical reality for neonatologists and ophthalmologists. Firstly, the screening process is highly resource-intensive, demanding the consistent availability of ophthalmologists trained and experienced in examining premature infants.[5] This requirement creates a critical barrier to access in many regions of the world, potentially leading to delayed diagnosis and irreversible vision loss. Secondly, the examination itself is an invasive procedure that can induce significant physiological stress—including pain, bradycardia, apnea, and fluctuations in blood pressure and oxygen saturation—in an already fragile patient population. Thirdly, the clinical assessment of ROP, which involves determining the stage, zone, and presence of plus disease, has an inherent degree of inter-observer variability, which can impact the timing and consistency of treatment decisions.

Most critically, however, the current screening model is fundamentally reactive. It is designed to detect pathological changes only after they have manifested, rather than proactively identifying those infants at the highest risk of progressing to severe, sight-threatening disease stages. This reactive stance necessitates a paradigm shift towards proactive risk prediction. The development and validation of objective, accessible, and cost-effective biomarkers could revolutionize ROP care, enabling individualized risk stratification, optimization of stressful examination schedules, and the potential guidance of preventive therapeutic strategies.[6]

The pathophysiology of ROP is classically described as a two-phase process. Phase I begins postnatally and involves the cessation of normal retinal vessel growth and the obliteration of existing capillaries.[7] This is driven by the abrupt transition from the physiologically hypoxic intrauterine environment to the relative hyperoxia of extrauterine life, often exacerbated by essential supplemental oxygen therapy. This vaso-obliteration leads to an avascular peripheral retina. Subsequently, Phase II is initiated by the metabolic demands of the developing retina, which, in the absence of adequate vasculature, becomes profoundly hypoxic. This ischemia triggers a pathological surge in pro-angiogenic factors, most notably Vascular Endothelial Growth Factor (VEGF), which promotes aberrant neovascularization. These new vessels are fragile, grow aberrantly into the vitreous, and can lead to fibrosis, tractional retinal detachment, and permanent blindness.

This two-phase model, while foundational, is now understood to be incomplete. A substantial body of evidence has firmly established that systemic inflammation is not merely a bystander but a critical upstream driver and modulator of both ROP phases. Preterm infants are uniquely susceptible to conditions that provoke a profound systemic inflammatory response, including sepsis, respiratory distress syndrome, necrotizing enterocolitis, and tissue injury from routine interventions.[8] This inflammatory state, characterized by the systemic release of pro-inflammatory cytokines, directly contributes to ROP pathogenesis by exacerbating retinal oxidative stress, damaging the delicate neurovascular unit, and amplifying the pathologic angiogenic response in Phase II.

This central role of inflammation provides a compelling biological rationale for investigating inflammatory biomarkers as predictive tools. The neutrophil-to-lymphocyte ratio (NLR), a simple index

derived from a standard differential white blood cell count, has emerged in recent years as a powerful, robust, and inexpensive marker of systemic inflammation.[9] The NLR reflects the dynamic balance between the innate immune system's primary effector cells (neutrophils) and the adaptive immune system's primary regulatory and memory cells (lymphocytes). An elevated NLR signifies a pro-inflammatory state characterized by a heightened, often dysregulated, innate immune response and a concurrently suppressed adaptive immune response—a state linked to poor outcomes across a vast spectrum of infectious, inflammatory, and oncologic diseases.

Given that the NLR is ubiquitously available from routine blood tests, virtually cost-free, and directly reflects the systemic inflammatory milieu implicated in ROP pathogenesis, it stands as an ideal candidate for a predictive biomarker. While individual studies have explored this association, a systematic synthesis that critically appraises the methodological quality of the evidence has been lacking.[10] This study aimed to systematically review and critically appraise the current body of evidence to evaluate the potential, consistency, and limitations of using the neutrophil-to-lymphocyte ratio (NLR) as a predictive biomarker for the development and severity of retinopathy of prematurity in preterm infants. This review distinguishes itself by conducting a formal risk-of-bias assessment of each included study and by placing a strong emphasis on interpreting the findings through the lens of the profound methodological heterogeneity that characterizes the existing literature, particularly concerning the timing of NLR measurement and the definition of ROP outcomes.

2. Methods

This systematic review was conducted and reported in strict adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement to ensure methodological transparency and completeness of reporting. Studies were deemed eligible for inclusion if they met criteria structured according to the Population, Exposure, Comparator, Outcome, and Study Design (PECOS) framework: Population: Preterm infants, defined as those born at <37 weeks of gestation, who were eligible for or undergoing ROP screening. No further restrictions on gestational age or birth weight were applied during the search phase to ensure comprehensive capture; Exposure: The measurement of the Neutrophil-to-Lymphocyte Ratio (NLR) from a peripheral blood sample at any postnatal time point; Comparator: A control or reference group of preterm infants without a diagnosis of ROP, or a reference group with milder stages of ROP for studies analyzing disease severity; Outcomes: The primary outcomes of interest were the diagnosis of ROP at any stage or, more specifically, the diagnosis of severe ROP. Severe ROP was defined according to criteria used in the primary studies, such as the presence of Stage 3 or higher disease, plus disease, or the need for treatment (laser photocoagulation or anti-VEGF therapy); Study Design: Eligible study designs included observational studies, such as retrospective or prospective cohort studies and case-control studies.

Full-text articles published in the English language were considered. The exclusion criteria were: review articles, editorials, case reports, conference abstracts, non-English articles, and studies that did not report a specific association between NLR and ROP. A systematic search was executed across four electronic databases: PubMed, ScienceDirect, ProQuest, and SpringerLink. The search was designed to identify all relevant articles published between January 1st, 2015, and December 31st, 2024. This timeframe was chosen to capture the most current evidence. The search strategy was developed to be highly sensitive, combining Medical Subject Headings (MeSH) and free-text keywords for two core concepts: "Retinopathy of Prematurity" and "Neutrophil-to-Lymphocyte Ratio". An example search string used for PubMed was: ("Retinopathy of Prematurity"[Mesh] OR "Retinopathy of Prematurity"[Title/Abstract]) AND ("Neutrophil-Lymphocyte Ratio"[Title/Abstract] OR "NLR"[Title/Abstract]). The full, detailed search strings for all four databases are provided in Supplementary

Table S1. To ensure comprehensive literature identification, the reference lists of all included articles and relevant narrative reviews were manually screened for any additional eligible studies. It is a limitation of this review that other major scientific databases, such as Embase and Web of Science, were not searched, which may have resulted in missing some relevant European or interdisciplinary literature. Furthermore, a formal search for grey literature was not conducted, which introduces a potential risk of publication bias.

Two reviewers independently executed the entire study selection process. All records identified through the database searches were imported into Zotero reference management software, and duplicate records were removed. The reviewers then independently screened the titles and abstracts of the remaining unique records against the pre-defined PECOS eligibility criteria. Any article deemed potentially relevant by at least one reviewer was advanced to the full-text review stage. The full texts were then retrieved and assessed independently by both reviewers for final inclusion. Any disagreements regarding study eligibility at either the abstract or full-text stage were resolved through discussion and consensus.

A standardized data extraction form, developed in Microsoft Excel, was used to collate data from the included studies. The two reviewers independently extracted key variables, including: study identifier and publication year; study design; population characteristics (total sample size, case/control numbers, mean/median GA and BW); the specific definition of the ROP outcome; details of the exposure, with a critical focus on the timing of blood collection for NLR measurement; key quantitative results such as mean/median NLR values, odds ratios (ORs) with 95% confidence intervals (CIs), and p-values; and the final NOS score. Data were cross-checked for accuracy and completeness after the extraction process was finished.

The methodological quality and risk of bias of each included observational study were independently assessed by the two reviewers using the Newcastle-Ottawa Scale (NOS), a validated tool designed for non-randomized studies. The NOS evaluates study quality across three key domains: 1) Selection (up to 4 stars): Assesses the adequacy of case and control definitions, the representativeness of the cases, and the selection and definition of controls; 2) Comparability (up to 2 stars): Assesses the extent to which studies controlled for important confounding factors. For this review, control for GA and/or BW was deemed essential for the award of one star, while control for other key clinical confounders, such as sepsis, was considered for the second star; and 3) Outcome/Exposure (up to 3 stars): Appraises the method of outcome or exposure ascertainment and the non-response rate.

Scores are summed to a maximum of 9 stars. Based on the final score, studies were categorized as Good Quality (7–9 stars), Fair Quality (4–6 stars), or Poor Quality (0–3 stars). All disagreements in scoring were resolved by consensus discussion. A quantitative meta-analysis of the results was considered but deemed inappropriate and potentially misleading due to the profound clinical and methodological heterogeneity observed across the included studies. Specifically, inconsistencies in the timing of NLR measurement, the definitions of ROP outcomes, and the statistical methods used in the primary studies precluded the pooling of effect estimates. Therefore, a structured narrative synthesis was employed to summarize and interpret the findings. The results are presented in tables and text, with an emphasis on comparing study characteristics, quality, and outcomes to identify patterns and inconsistencies in the evidence.

Due to the small number of included studies (n=6), a formal statistical assessment for publication bias was not performed. Such methods are known to be underpowered and unreliable with fewer than 10 studies. The potential for publication bias—whereby smaller studies with null or negative findings are less likely to be published—is therefore acknowledged as a significant and unquantified limitation of this review and its conclusions.

3. Results

The systematic database search yielded a total of 32 records. After the removal of 7 duplicate records, 25 unique articles were screened based on their titles and abstracts. This initial screening led to the exclusion of 19 articles that were clearly irrelevant (focused on different biomarkers or diseases), were not original research (reviews, editorials), or did not assess the specified association between NLR and ROP. The full texts of the remaining 6 articles were retrieved for a detailed eligibility assessment. All 6 of these articles met the pre-specified inclusion criteria and were included in the final qualitative synthesis. The PRISMA flow diagram detailing the study selection process is shown in Figure 1.

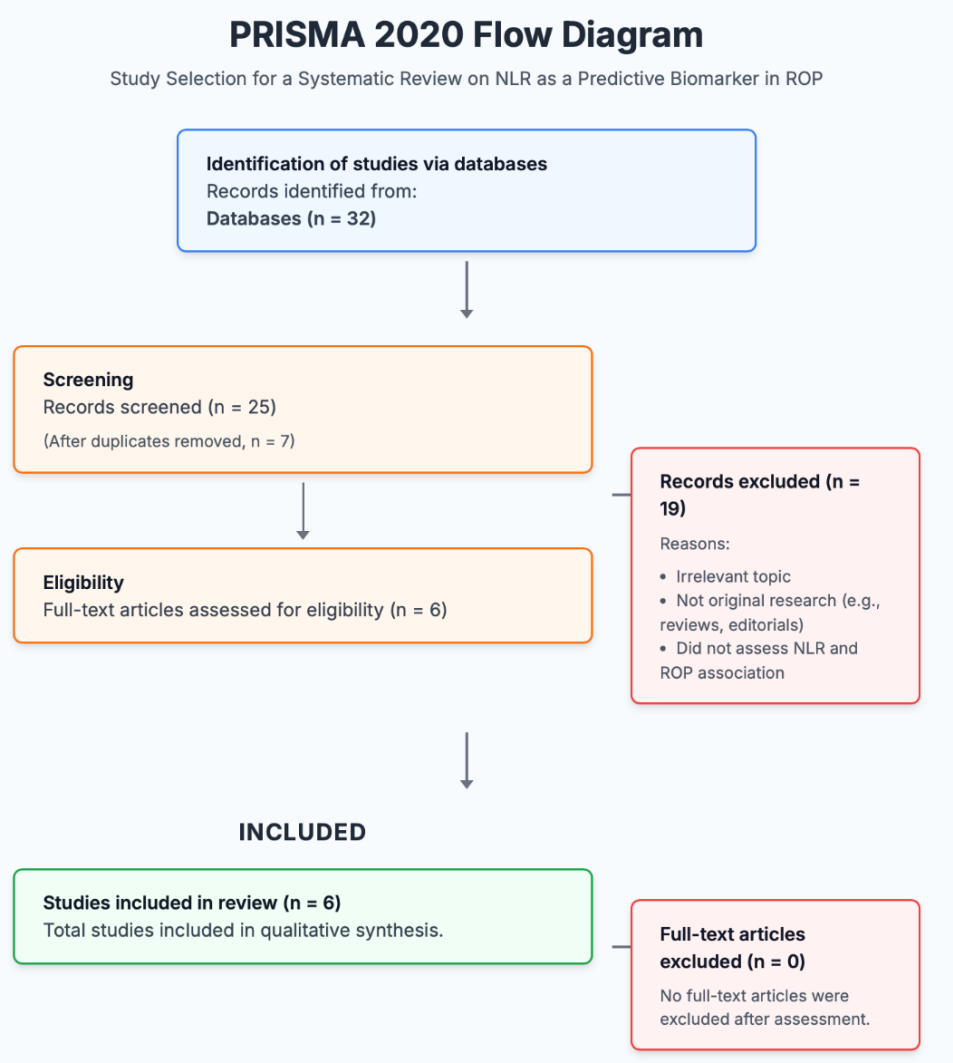

Figure 1. PRISMA 2020 flow diagram of study selection.

The six included studies were all retrospective in design and were published between 2017 and 2025. They involved a collective, though incompletely reported, sample of 1,065 preterm infants. The methodological quality of the evidence, as appraised by the NOS, was determined to be low-to-moderate, with scores ranging from 5 to 7 out of 9. This categorized four studies as 'Fair' quality and two as 'Good' quality. A detailed breakdown of the characteristics and quality assessment of each study is presented in Table 1.

A primary finding of this review is the profound heterogeneity across study methodologies, which severely limits the ability to draw cohesive conclusions. This inconsistency is particularly stark in two critical areas: 1) ROP Outcome Definition: The studies were split in their focus. Half analyzed the development of any stage of ROP as the primary outcome, while the other half focused on the more clinically urgent outcome of severe, treatment-requiring ROP; and 2) Timing of Blood Draw: This crucial variable, which dictates the physiological context of the NLR measurement, was either not reported or varied widely. Three of the six studies, including two that focused on severe ROP, failed to state when the blood for NLR analysis was collected. For those that did report timing, it ranged from the first 72 hours of life to after the first week. This lack of standardization is a critical flaw in the evidence base.

Furthermore, significant reporting gaps were evident in the primary studies. Study 1 was rated as 'Good' quality despite the manuscript noting that the gestational age and birth weight of the infant population were "not detailed". Study 6 failed to report its total sample size. These omissions of fundamental baseline data call into question the quality of the primary research and complicate any attempt at synthesis.

Table 1. Characteristic and quality assessment of included studies.

Systematic Review: Included Studies

Table 1: Characteristics and Quality Assessment

STUDY ID	DESIGN & POPULATION	ROP OUTCOME DEFINITION	TIMING OF BLOOD DRAW	NOS SCORE	QUALITY
Study 1	**Retrospective Case-Control** 348 infants *GA/BW not detailed*	Severe ROP	*Not Stated*	7 / 9	Good
Study 2	**Retrospective Case-Control** 303 infants, Mean GA ~30 wks	Any ROP / Severity	*Not Stated*	6 / 9	Fair
Study 3	**Retrospective Case-Control** 153 infants, Mean BW ~1250g	Any ROP	First 72 hours	6 / 9	Fair
Study 4	**Retrospective Cohort** 163 infants, Mean GA ~31 wks	Any ROP	After first week	6 / 9	Fair
Study 5	**Retrospective Cohort** 98 infants, Mean GA ~28 wks	Severe ROP	*Not Stated*	5 / 9	Fair
Study 6	**Retrospective Case-Control** *Size not reported*	Any ROP	*Not Stated*	5 / 9	Fair

Abbreviations: GA: Gestational Age; BW: Birth Weight; ROP: Retinopathy of Prematurity; NOS: Newcastle-Ottawa Scale; wks: weeks.

A structured narrative synthesis was conducted due to the heterogeneity outlined above. Rather than relying on simplistic vote-counting, this synthesis describes the findings from each study in the context of its specific methodology and quality. The key findings regarding the association between inflammatory markers and ROP are summarized in Table 2.

Table 2. Summary of key findings and reported statistics on the association between inflammatory markers and ROP.

Systematic Review: Key Findings

Summary of Association between Inflammatory Markers and ROP

STUDY ID	FOCUS OUTCOME	KEY FINDINGS & INTERPRETATION	REPORTED SIGNIFICANCE
Study 1	Severe ROP	**Reported a statistically significant predictive association for NLR.** Other markers (PLR, MLR) were also noted as elevated.	Significant
Study 2	Any ROP / Severity	**NLR was significantly higher in the ROP group.** A direct correlation was found between increasing NLR values and ROP severity.	Significant
Study 3	Any ROP	**Observed a significant increase in NLR in infants diagnosed with any stage of ROP.**	Significant
Study 4	Any ROP	**Primary focus was on a different marker (LMR).** Authors noted NLR **tended to increase**, but this was not statistically significant.	Not Significant (NLR)
Study 5	Severe ROP	**Primary focus was on Systemic Inflammation Index (SII).** Found SII was significantly higher in severe ROP; NLR was not the primary endpoint.	Indirect (SII)
Study 6	Any ROP	**Found no statistically significant difference in NLR between ROP and non-ROP groups.**	Not Significant

Abbreviations: ROP: Retinopathy of Prematurity; NLR: Neutrophil-to-Lymphocyte Ratio; PLR: Platelet-to-Lymphocyte Ratio; MLR: Monocyte-to-Lymphocyte Ratio; LMR: Lymphocyte-to-Monocyte Ratio; SII: Systemic Immune-Inflammation Index.

The narrative synthesis reveals a complex and inconsistent evidence base. Three studies reported a direct, statistically significant association between an elevated NLR and ROP. Study 1 identified this link specifically with severe, treatment-requiring ROP, and Study 2 suggested a "dose-response" relationship where NLR values increased with ROP severity. Study 3 also found a significant increase in NLR in infants with any ROP. However, the strength of these findings is tempered by their methodological limitations. Two of these three studies (Study 1 and Study 2) failed to report the timing of the blood draw, a critical variable that fundamentally limits the clinical interpretation and comparability of the results.

Two studies presented more ambiguous results. Study 4 primarily focused on a different biomarker, the lymphocyte-to-monocyte ratio (LMR). While its authors noted that NLR also "tended to increase," this observation did not reach statistical significance. Study 5 focused on the Systemic Immune-Inflammation Index (SII), a composite marker that includes neutrophils, and found it was significantly higher in severe ROP. While this suggests systemic inflammation is involved, it is not a direct measure of NLR's independent predictive value. To categorize this as a positive study for NLR would be a misinterpretation.

One study (Study 6) directly compared NLR between ROP and non-ROP groups and found no statistically significant difference. Although the primary authors noted a "trend" toward elevated markers, this finding did not meet the threshold for statistical significance. This negative finding is an important component of the overall evidence base. Its value is, however, limited by its 'Fair' quality rating and the failure to report the total sample size, which prevents any external assessment of its statistical power.

In summary, the narrative synthesis does not support a confident conclusion. While some retrospective data suggests a link, the evidence is undermined by studies with null findings, indirect evidence, and, most importantly, pervasive methodological flaws and reporting gaps across the entire body of literature.

4. Discussion

This systematic review provides a critical appraisal of the current evidence on NLR as a predictive biomarker for ROP. The principal finding is that the existing literature, which is composed exclusively of small, retrospective studies, is of low-to-moderate quality and is defined by profound methodological heterogeneity.[11] While some studies report a statistically significant association between an elevated NLR and ROP risk or severity, this finding is not consistent across all studies and is severely weakened by critical flaws, most notably the lack of standardized or even reported timing for NLR measurement. Therefore, this review concludes that the current evidence base is immature and insufficient to support any firm conclusions about the clinical utility of NLR in predicting ROP.

The hypothesis that NLR could predict ROP is anchored in a compelling and deep biological rationale.[12] An elevated NLR provides a biological snapshot of an immune system in a state of dysregulation: a hyperactive, destructive innate arm (neutrophilia) and a suppressed, ineffective adaptive arm (lymphopenia). This specific pattern of immune response creates a microenvironment highly conducive to the development and progression of ROP.

The neutrophilia component signifies a state of intense systemic inflammation. Activated neutrophils contribute directly to ROP pathogenesis through several mechanisms.[13] They generate a massive oxidative burst, releasing reactive oxygen species (ROS) that cause collateral damage to the delicate, developing retinal neurovascular unit.[14] They release potent proteolytic enzymes from their granules, which degrade the extracellular matrix and destabilize retinal capillaries. Furthermore, through NETosis, neutrophils expel webs of DNA and cytotoxic proteins known as Neutrophil Extracellular Traps (NETs), which are intensely pro-inflammatory and can physically occlude retinal microvessels, worsening the ischemia that drives pathologic neovascularization.[14] Concurrently, the relative lymphopenia seen in a high-NLR state reflects a suppressed or dysfunctional adaptive immune system, which is critical for resolving inflammation and providing regulatory oversight. This implies an impaired ability to terminate the initial neutrophil-driven inflammatory cascade, allowing retinal damage to proceed unchecked.

While this biological model is powerful, it is crucial to starkly contrast this theoretical framework with the weaknesses of the actual clinical evidence synthesized in our review. The human studies included here are fraught with inconsistencies and flaws that prevent the validation of this biological hypothesis in a clinical setting. The compelling plausibility of the mechanism cannot substitute for high-quality clinical data. The central challenge moving forward is to bridge the gap between this strong biological rationale and the current weak, heterogeneous clinical evidence.[15]

The conclusions of this review must be interpreted in the context of several major limitations, stemming from both the primary studies and the review process itself: 1) Exclusive Reliance on Retrospective Data: All six included studies were retrospective, a design inherently prone to selection bias, recall bias, and unmeasured confounding; 2) Profound Methodological Heterogeneity: As detailed in the results, the included studies varied so significantly in their outcome definitions and, most critically, in the timing of NLR measurement, that a meaningful comparison or synthesis was nearly impossible. This lack of protocol standardization is the single greatest weakness of the existing literature; 3) Poor Quality and Reporting of Primary Studies: Several studies failed to report fundamental data, such as the baseline GA/BW of the population or the total sample size, severely compromising their scientific validity; 4) Limitations of the Review Process: This review was limited to English-language publications, potentially missing relevant data from other regions.[16] The search strategy did not include several major databases or a formal search for grey literature. Furthermore, the review protocol was not prospectively registered; and 5) Inability to Assess Publication Bias: A formal assessment of publication bias could not be performed due to the small number of studies. It is highly plausible that smaller studies

with null findings have gone unpublished, which would skew the available evidence towards a positive association. This is a critical, unquantified limitation.[17]

The primary clinical implication of this systematic review is that NLR is not ready for clinical use in the management of ROP.[18] It should not be used as a standalone diagnostic tool, should not replace funduscopic examination, and its current evidence base provides no guidance for its integration into risk stratification models. Its profound lack of specificity is a major barrier; sepsis, necrotizing enterocolitis, and numerous other conditions common in preterm infants will also elevate NLR, making it impossible to attribute a high NLR solely to ROP risk. The vision of using NLR within a multi-biomarker, algorithm-based predictive model remains a valid long-term goal. However, the current evidence is far too preliminary to even begin designing such a model. The path forward is not clinical implementation but a dedicated and rigorous research effort.

The absolute priority is the execution of large-scale, multicenter, prospective cohort studies. To be successful, these future investigations must be designed with meticulous methodology to overcome the flaws of the past: Standardized Protocols: They must implement strict, uniform time points for serial blood collection (24 hours, 72 hours, 1 week, 2 weeks, and monthly thereafter) to map the temporal dynamics of NLR; Rigorous Confounder Control: Comprehensive data on all potential confounders—especially culture-proven sepsis, respiratory support, and nutritional status—must be collected to allow for advanced statistical modeling that can isolate the independent predictive value of NLR; Uniform Outcome Assessments: Standardized definitions for ROP, focusing specifically on the most clinically relevant outcome of treatment-requiring ROP (Type 1 ROP), must be used across all centers. Only through such rigorous investigation can we validate or refute the findings of these initial retrospective reports, establish clinically meaningful NLR thresholds, and build the robust evidence base needed to confidently determine the true role, if any, for this simple biomarker in the future of ROP care.[19]

5. Conclusion

This systematic review, which includes a formal risk-of-bias assessment, consolidates the existing literature on the neutrophil-to-lymphocyte ratio as a potential predictive biomarker for retinopathy of prematurity. The findings indicate that while there is a strong biological rationale for a link between elevated NLR and ROP, the current clinical evidence is sparse, inconsistent, and derived exclusively from low-to-moderate quality retrospective studies with profound methodological flaws. The heterogeneity across studies, particularly in the timing of NLR measurement, is so significant that it precludes any firm conclusions or recommendations for clinical practice. The promise of NLR as an accessible, low-cost biomarker is immense, but its potential remains unrealized and unproven. The research mandate is clear: the hypothesis generated by these initial studies must now be tested in high-quality, large-scale prospective cohort studies with standardized protocols. Until such evidence is available, NLR has no established role in the routine screening, risk stratification, or management of infants at risk for ROP.

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