

Neutrophil-To-Lymphocyte Ratio and Severity of Hypertensive Retinopathy: The Potential Role of Systemic Inflammation in Retinal Microvascular Injury

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Abstract

Background: Hypertension is a major cause of cardiovascular, renal, neurological and ocular target-organ damage. Hypertensive retinopathy represents a spectrum of retinal microvascular abnormalities resulting from sustained or severe elevation of blood pressure. Although retinal arteriolar narrowing, arteriovenous crossing changes, haemorrhages, cotton-wool spots, exudates and optic disc swelling are well recognized manifestations, increasing evidence indicates that hypertension is also associated with chronic low-grade systemic inflammation. The neutrophil-to-lymphocyte ratio (NLR), calculated from the absolute neutrophil and lymphocyte counts obtained from a routine full blood count, has emerged as an inexpensive marker of systemic inflammatory and physiological stress. However, the relationship between NLR and the severity of hypertensive retinopathy remains insufficiently explored.

Objective: This review examines the biological plausibility and available evidence linking NLR with hypertensive retinopathy, discusses mechanisms through which systemic inflammation may contribute to retinal microvascular injury, and proposes a framework for investigating whether NLR is associated with the severity of hypertensive retinopathy.

Methods: A narrative review of relevant peer-reviewed literature was undertaken, with emphasis on studies addressing NLR, systemic inflammation, hypertension, hypertensive target-organ damage, retinal microvascular disease and inflammatory hematological indices in retinal vascular disorders. Evidence from systematic reviews, meta-analyses, clinical studies and contemporary hypertension and ophthalmic literature was considered.

Discussion: Hypertension is increasingly recognized as an inflammatory and immune-mediated vascular disorder. Neutrophil activation, lymphocyte alterations, oxidative stress, endothelial dysfunction, vascular remodeling and inflammatory cytokine signaling may contribute to hypertension-associated vascular injury. The retina provides a unique opportunity to visualize microvascular consequences of systemic hypertension. Although direct evidence specifically relating NLR to graded hypertensive retinopathy is currently limited, studies in hypertension demonstrate higher NLR among hypertensive individuals, while ophthalmic studies show increased NLR in retinal artery and vein occlusive diseases. These observations provide a biologically plausible basis for investigating NLR as a potential marker of hypertensive retinal microvascular injury. Importantly, NLR is nonspecific and is affected by age, sex, smoking, obesity, infection, medications, diabetes and other inflammatory conditions.

Conclusion: NLR represents a readily available, inexpensive haematological index with potential relevance to hypertensive retinopathy. A well-designed prospective or analytical cross-sectional study combining standardized retinal grading with full blood count, blood pressure measurements and assessment of major confounders could determine whether NLR is independently associated with retinopathy severity. Such research may provide useful evidence for collaboration between optometry, ophthalmology, Haematology and medical laboratory science, particularly in resource-constrained settings.

Keywords: neutrophil-to-lymphocyte ratio; hypertension; hypertensive retinopathy; retinal microvascular disease; systemic inflammation; neutrophils; lymphocytes; retinal vascular injury; hematological biomarkers

Introduction

Hypertension is one of the most important chronic cardiovascular disorders worldwide. Its clinical importance extends far beyond the numerical elevation of arterial blood pressure. Persistent elevation of blood pressure places mechanical and

biological stress on the vascular system and may progressively damage the heart, brain, kidneys, peripheral circulation and retina. The 2024 European Society of Cardiology guidelines emphasize that cardiovascular risk increases continuously with increasing blood pressure rather than appearing abruptly at a single numerical threshold [1].

The retina is particularly interesting in the study of hypertension because its blood vessels can be directly observed *in vivo*. Retinal arterioles and venules provide an accessible window into the microcirculation and may demonstrate vascular changes associated with chronic systemic hypertension. Hypertensive retinopathy encompasses a range of retinal vascular abnormalities, from subtle arteriolar narrowing and arteriovenous nicking to haemorrhages, cotton-wool spots, exudates, retinal oedema and optic disc swelling in severe cases [2-4]. For many years, the pathophysiology of hypertensive retinopathy was described predominantly in mechanical terms. Sustained elevation of blood pressure was thought to cause vasoconstriction, arteriolar sclerosis, endothelial injury and disruption of the blood-retinal barrier. This model remains important, but it is increasingly evident that vascular inflammation, oxidative stress, immune-cell activation and endothelial dysfunction also participate in hypertensive vascular injury. This shift in understanding provides an opportunity to examine simple inflammatory biomarkers in patients with hypertension. One such biomarker is the neutrophil-to-lymphocyte ratio (NLR). NLR is calculated by dividing the absolute neutrophil count by the absolute lymphocyte count: $\text{NLR} = \text{absolute neutrophil count} / \text{absolute lymphocyte count}$

The ratio is attractive because both components are obtained from the same full blood count with differential. It therefore requires no specialized assay and adds little cost to routine laboratory testing. Zahorec originally described the neutrophil-to-lymphocyte ratio as a simple indicator of systemic inflammation and physiological stress, and the marker has subsequently been investigated across numerous medical disciplines [5-6]. The biological rationale for NLR is relatively straightforward. Neutrophilia may reflect activation of the innate immune response, while lymphopenia may reflect physiological stress, altered adaptive immune activity or redistribution of lymphocytes. Consequently, an increased NLR may represent the combined effect of increased inflammatory activity and relative suppression or redistribution of lymphocytes. Several studies have associated elevated NLR with cardiovascular disease, hypertension and cardiovascular mortality. A systematic review and meta-analysis involving 38 studies and 76,002 participants found that higher NLR was associated with coronary artery disease, acute coronary

syndrome, stroke and composite cardiovascular event [7]. More recently, a systematic review and meta-analysis involving 10 studies and 78,194 participants reported that NLR was associated with the occurrence of hypertension and with all-cause and cardiovascular mortality among hypertensive patients [8]. Importantly, the retina is also susceptible to inflammatory and vascular processes. Studies of retinal vascular occlusion have demonstrated increased NLR in patients with retinal artery occlusion and retinal vein occlusion [9-12]. However, a crucial gap remains. Does NLR increase progressively with the severity of hypertensive retinopathy? This question is clinically interesting because it brings together three areas that are often investigated separately:

1. systemic hypertension;
2. systemic inflammation; and
3. retinal microvascular injury.

If NLR were shown to correlate independently with hypertensive retinopathy severity, it could provide a simple hematological indicator of systemic inflammatory burden in patients undergoing retinal assessment.

The purpose of this review is therefore to examine the scientific basis for this proposed relationship and to develop a framework for future research.

Hypertension as a Systemic Vascular and Inflammatory Disorder

Hypertension is commonly defined clinically according to blood pressure thresholds, but the biological consequences of elevated blood pressure develop along a continuum.

The 2024 European Society of Cardiology guideline defines hypertension as confirmed office systolic blood pressure of at least 140 mmHg and/or diastolic blood pressure of at least 90 mmHg, while emphasizing that cardiovascular risk rises continuously across the blood-pressure spectrum [1]. The chronic elevation of arterial pressure exposes vascular endothelial cells and smooth-muscle cells to abnormal mechanical forces. Shear stress, cyclic stretch and pressure overload can alter endothelial function and promote vascular remodeling.

The vascular endothelium is not merely a passive barrier. It participates actively in regulation of vascular tone, coagulation, leukocyte adhesion, permeability and inflammatory signaling. Under normal conditions, endothelial cells produce vasodilatory and anti-inflammatory mediators such as nitric oxide and prostacyclin. Hypertension can disrupt this balance.

Reduced nitric oxide bioavailability, increased oxidative stress and activation of inflammatory signaling may promote endothelial dysfunction. Once endothelial integrity is compromised, circulating leukocytes can interact more readily with the vascular wall.

Neutrophils may adhere to activated endothelium, migrate into tissues and release proteolytic enzymes, reactive oxygen species and other inflammatory mediators. Neutrophils are now recognized as active participants in cardiovascular inflammation rather than merely passive markers of disease [13]. Lymphocytes also participate in vascular inflammation. Different lymphocyte subsets can exert pro-inflammatory or regulatory effects. Alteration in lymphocyte number or function may therefore modify the inflammatory environment.

The NLR attempts to capture some of these opposing cellular processes in a single numerical index.

Understanding the Neutrophil-to-Lymphocyte Ratio

NLR is a derived parameter rather than a directly measured analyte.

For example, if a patient has:

absolute neutrophil count = $5.0 \times 10^9/L$

absolute lymphocyte count = $2.0 \times 10^9/L$

then:

$$NLR = 5.0 / 2.0 = 2.5$$

A patient with:

neutrophils = $7.0 \times 10^9/L$

lymphocytes = $1.5 \times 10^9/L$

would have:

$$NLR = 7.0 / 1.5 = 4.67$$

The second patient therefore has a considerably higher NLR.

The significance of this ratio is not that an NLR of a particular value automatically diagnoses inflammation. Rather, the value provides a relative indication of the balance between circulating neutrophils and lymphocytes.

NLR has several practical advantages.

First, it is inexpensive.

Second, it can be obtained from a routine full blood count.

Third, it does not require a dedicated inflammatory biomarker assay.

Fourth, it can be measured in settings where more sophisticated biomarkers such as interleukin-6, tumor necrosis factor-alpha or high-sensitivity C-reactive protein may not be readily available.

These characteristics are particularly relevant in low- and middle-income settings. However, NLR also has important limitations.

It is not disease-specific.

NLR may rise in:

Acute infection; chronic inflammatory disease; malignancy; cardiovascular disease; tissue injury; psychological or physiological stress; smoking; obesity; corticosteroid exposure; and other conditions.

Therefore, NLR should not be interpreted in isolation.

Biological Basis of NLR

The two components of NLR have different biological meanings.

Neutrophils

Neutrophils are major components of innate immunity. They are rapidly recruited to sites of infection and tissue injury.

Activated neutrophils can release: reactive oxygen species; myeloperoxidase; elastase; proteases; inflammatory cytokines; and neutrophil extracellular traps. These mechanisms are beneficial during host defence but can contribute to tissue injury when excessively activated or chronically stimulated.

Cardiovascular research has demonstrated important relationships between neutrophils, endothelial dysfunction, vascular inflammation and atherosclerosis [13]. In hypertension, neutrophils may therefore contribute to a broader inflammatory environment affecting systemic blood vessels.

Lymphocytes

Lymphocytes include T cells, B cells and natural killer cells. Their functions include immune regulation, antibody production, cellular immunity and immune surveillance. A reduction in circulating lymphocytes can occur during physiological stress through neuroendocrine mechanisms and redistribution of lymphocytes between circulating blood and tissues. Consequently, a high NLR may reflect both increased innate inflammatory activity and reduced circulating adaptive immune representation. This dual interpretation partly explains why NLR can provide more information than neutrophil count alone.

NLR and Hypertension

The relationship between NLR and hypertension has been investigated in numerous studies. A 2023 systematic review and meta-analysis included 21 studies examining NLR in hypertensive and normotensive individuals. The pooled analysis found

significantly higher NLR among hypertensive individuals, with a weighted mean difference of 0.40. NLR was also higher among non-dipping compared with dipping hypertensive patients [8-14]. This finding is important because the non-dipping blood pressure pattern is associated with cardiovascular risk and may reflect abnormal autonomic and vascular regulation. The association between NLR and blood pressure variability has also been investigated. Barış Kılıçaslan et al. examined the relationship between NLR and blood pressure variability in hypertensive and normotensive individuals [15]. The study is relevant because fluctuating blood pressure may expose vascular tissues to repeated haemodynamic stress. More recent evidence has extended the association between NLR and hypertension to target-organ damage. In a 2025 study of 346 patients with essential hypertension, Francesca Petramala and colleagues reported that higher NLR was associated with higher blood pressure, use of multiple antihypertensive medications and a greater prevalence of subclinical organ damage, including increased left ventricular mass, carotid atherosclerosis and microalbuminuria [16]. Taken together, these observations suggest that NLR may reflect more than the presence of hypertension itself. It may also be related to the degree of vascular or systemic injury associated with hypertension. This raises the possibility that the retina could represent another target organ in which this relationship may be observed.

Hypertension and Retinal Microvascular Injury

The retinal circulation is particularly sensitive to changes in systemic blood pressure. When blood pressure rises, retinal arterioles initially undergo autoregulatory vasoconstriction. If hypertension persists, structural changes may develop in the vascular wall.

These changes can include: arteriolar narrowing; increased arteriolar wall reflectivity; arteriovenous nicking; vascular tortuosity; endothelial dysfunction; breakdown of the blood-retinal barrier; retinal haemorrhage; cotton-wool spots; hard exudates; retinal oedema; and optic disc swelling in severe cases. The retina therefore provides a visual record of microvascular injury. A major review of hypertensive retinopathy notes that hypertension may produce vascular changes ranging from mild arteriolar narrowing to severe retinopathy involving hemorrhages, exudates, cotton-wool spots and optic

disc oedema [3]. This spectrum of disease makes hypertensive retinopathy suitable for investigating relationships with systemic biomarkers.

Classification of Hypertensive Retinopathy

The classical Keith-Wagener-Barker classification divides hypertensive retinopathy into four grades.

Grade I

Mild generalized arteriolar narrowing or sclerosis.

Grade II

More marked arteriolar sclerosis, focal narrowing and arteriovenous crossing abnormalities.

Grade III

Grade II changes accompanied by retinal haemorrhages, exudates, cotton-wool spots and/or retinal oedema.

Grade IV

Grade III changes accompanied by optic disc oedema/papilloedema.

The classification remains historically important and is still frequently cited [2].

However, there are concerns about reproducibility, particularly in distinguishing early grades. A study comparing the Keith-Wagener-Barker system with the simplified Mitchell-Wong system found better observer agreement with the simplified system and noted that early grades of the classical system may be difficult to distinguish [17]. Therefore, a contemporary research study should specify the grading system before recruitment begins.

The Mitchell-Wong Classification

The simplified classification proposed by Wong and Mitchell groups hypertensive retinal changes into: none; mild; moderate; and severe.

Mild retinopathy includes signs such as generalized or focal arteriolar narrowing, arteriovenous nicking and arteriolar wall changes.

Moderate retinopathy includes retinal haemorrhages, microaneurysms, cotton-wool spots and hard exudates.

Severe retinopathy includes moderate retinopathy with optic disc swelling [3,18].

For a study investigating NLR and severity, the Mitchell-Wong classification may be attractive because it reduces ambiguity between early grades. However, the investigators may also record the individual retinal signs rather than relying only on a composite grade. This would allow analysis of whether NLR is associated particularly with: arteriolar narrowing; haemorrhage; cotton-wool spots; exudates; or optic disc swelling.

Pathophysiological Link Between NLR and Hypertensive Retinopathy

The proposed relationship between NLR and hypertensive retinopathy can be conceptualized as a chain of interacting events:

Hypertension



Mechanical vascular stress



Endothelial dysfunction



Oxidative stress and inflammatory activation



Neutrophil activation + lymphocyte alterations



Increased NLR



Microvascular endothelial injury



Retinal arteriolar changes



Retinal ischemia and vascular leakage



Increasing hypertensive retinopathy severity.

This pathway should be regarded as a biological hypothesis, not an established causal sequence. The existing evidence demonstrates separate links in the pathway, but direct evidence connecting NLR with graded hypertensive retinopathy remains limited. That gap is precisely what makes the proposed research worthwhile.

Oxidative Stress as a Common Mechanism

Oxidative stress is an important mechanism in hypertension-associated vascular injury. Excessive production of reactive oxygen species can reduce nitric oxide bioavailability and impair endothelial function. Oxidative stress may also activate inflammatory pathways and increase leukocyte-endothelial interactions. The retina is particularly vulnerable because it has high metabolic activity and substantial oxygen requirements. When retinal vascular autoregulation becomes impaired, oxidative and inflammatory mechanisms may compound vascular dysfunction. Thus, systemic inflammation reflected by NLR may potentially contribute to the same biological environment that promotes retinal microvascular injury.

Endothelial Dysfunction

Endothelial dysfunction is a central feature of hypertension. The healthy endothelium maintains

vascular relaxation, regulates permeability and suppresses inappropriate leukocyte adhesion.

Hypertension can disturb these functions. Activated endothelial cells express adhesion molecules that facilitate interaction with circulating leukocytes. Neutrophils can adhere to and migrate through the endothelium. Once activated, they can release substances capable of damaging endothelial structures.

This mechanism has obvious relevance to retinal vessels. Damage to retinal endothelial cells may increase vascular permeability and allow plasma components to enter retinal tissue. Clinically, this can contribute to retinal hemorrhages, exudation and oedema.

Neutrophils and Vascular Injury

The traditional description of neutrophils as short-lived cells primarily involved in acute infection is incomplete. Contemporary cardiovascular research recognizes neutrophils as active regulators of vascular inflammation [13].

Neutrophils can participate in: endothelial injury; vascular remodeling; atherosclerotic plaque inflammation; thrombosis; oxidative stress; and neutrophil extracellular trap formation.

In hypertension, these processes may contribute to vascular stiffness and endothelial dysfunction.

Because retinal vessels are part of the systemic vascular system, similar inflammatory processes could potentially occur in the retinal circulation. The extent to which circulating NLR captures these local retinal processes remains uncertain. This is an important reason why NLR should be viewed as a systemic marker rather than a direct measurement of retinal inflammation.

Lymphocytes and Hypertensive Vascular Disease

Lymphocytes have also been implicated in hypertension. Different T-cell populations may have different effects on vascular inflammation. Pro-inflammatory T-cell responses can promote cytokine production and vascular dysfunction, whereas regulatory T cells can suppress excessive inflammation. Thus, a reduced lymphocyte count may not simply represent an absence of immune activity. It may reflect redistribution, physiological stress or changes in immune regulation. When combined with neutrophil elevation, lymphocyte reduction produces an increased NLR. This ratio may therefore provide a broad indication of the balance

between innate inflammatory activation and adaptive immune regulation.

NLR and Retinal Vascular Disease: Indirect Ophthalmic Evidence

Although research specifically on hypertensive retinopathy is limited, several ophthalmic studies provide indirect support for the proposed relationship. Retinal artery occlusion and retinal vein occlusion are important retinal vascular disorders associated with vascular risk factors and inflammatory mechanisms.

In patients with retinal artery occlusion, studies have reported significantly increased NLR compared with controls. One study involving 97 participants reported mean NLR values of 2.85 ± 1.70 in retinal artery occlusion compared with 1.63 ± 0.59 in controls [19]. Another study involving retinal artery and vein occlusion reported higher NLR in both groups, with NLR particularly elevated among patients with retinal artery occlusion [20]. A 2025 meta-analysis involving 1,444 participants from eight studies found significantly elevated NLR among patients with retinal artery occlusion, with a pooled standardized mean difference of 0.88 [21]. These findings do not establish that NLR causes hypertensive retinopathy.

They do, however, demonstrate that inflammatory haematological indices are associated with clinically important retinal vascular diseases.

NLR and Retinal Vein Occlusion

The evidence is also substantial for retinal vein occlusion. A case-control study by researchers investigating complete blood count-derived inflammatory indices found significantly higher white blood cell counts, neutrophil counts and NLR among patients with retinal vein occlusion compared with controls [22].

The NLR was also the strongest of the evaluated inflammatory indices in their receiver operating characteristic analysis.

Similarly, a systematic review and meta-analysis of eight studies involving 1,059 patients found that NLR was significantly elevated among patients with retinal vein occlusion, with a pooled mean difference of 0.63 [23]. These findings are important because retinal vein occlusion involves vascular endothelial dysfunction, inflammation and thrombosis. The relationship between NLR and retinal vascular occlusion therefore supports the broader concept that

systemic inflammatory status may be reflected in retinal vascular disease.

Why Hypertensive Retinopathy May Be Different

It is important not to assume that findings from retinal vascular occlusion automatically apply to hypertensive retinopathy. Retinal vein occlusion is an acute or subacute vascular event involving thrombosis and/or impaired venous drainage. Hypertensive retinopathy is generally a manifestation of chronic or severe blood-pressure-related microvascular injury. The biological processes overlap but are not identical. Therefore, studies of NLR in retinal vascular occlusion provide supporting biological evidence, not direct evidence of the NLR-hypertensive-retinopathy relationship. This distinction should be clearly maintained in any journal manuscript.

NLR and Retinal Severity

The most important unanswered question is whether NLR increases as hypertensive retinopathy progresses. A possible pattern would be:

Retinal status Hypothetical inflammatory pattern.

No retinopathy Lower NLR.

Mild retinopathy Slightly increased NLR.

Moderate retinopathy Higher NLR.

Severe retinopathy Highest NLR.

This is a research hypothesis, not a finding that should be reported before data are collected.

If a future study demonstrates such a gradient, it would strengthen the argument that systemic inflammatory burden is related to retinal microvascular injury. However, the relationship may not be linear. For example, NLR could increase sharply only among patients with moderate or severe retinal disease. Alternatively, NLR could be elevated in hypertension generally but show little difference across retinopathy grades. Either outcome would be scientifically valuable.

Hypertensive Retinopathy as a Marker of Target-Organ Damage

Retinal vascular changes should not be regarded solely as an ocular phenomenon.

Hypertensive retinopathy may reflect systemic microvascular damage. Retinal microvascular abnormalities have been investigated in relation to cardiovascular, renal and neurological outcomes.

A Nigerian study of treated hypertensive patients found a high prevalence of target-organ damage, including left ventricular hypertrophy, chronic kidney disease, diabetic nephropathy, heart failure and

cerebrovascular disease [24]. This emphasizes the importance of recognizing hypertension as a systemic disorder. If NLR correlates with retinal severity, it may potentially represent a broader inflammatory marker of hypertensive target-organ injury.

Blood Pressure Severity and NLR

Any study of NLR and hypertensive retinopathy must account for the actual severity and duration of hypertension. Blood pressure should ideally be measured using standardized procedures.

Important parameters include: systolic blood pressure; diastolic blood pressure; pulse pressure; mean arterial pressure.

Where resources permit, 24-hour ambulatory blood pressure monitoring would provide additional information concerning: daytime blood pressure; nocturnal blood pressure; dipping status; blood pressure variability. This is relevant because a single clinic measurement may not accurately represent the patient's cumulative hemodynamic exposure.

Duration of Hypertension

The duration of hypertension is another important variable. Two individuals may have identical blood pressure readings but very different cumulative exposure to hypertension. A patient who has had hypertension for 15 years may have substantially more vascular remodeling than someone diagnosed six months previously. Therefore, duration of hypertension should be recorded. Antihypertensive treatment history should also be documented, including: number of medications; drug classes; treatment duration; adherence; previous hypertensive crises. These factors may influence both NLR and retinal disease.

Diabetes as a Major Confounder

Diabetes mellitus must be carefully considered. Diabetes itself can cause retinal microvascular injury and systemic inflammation. A patient with both diabetes and hypertension may have retinal abnormalities caused by diabetic retinopathy, hypertensive retinopathy or a combination of both. Therefore, diabetic patients should either be excluded from the primary study or analyzed separately.

If included, the study should measure: fasting plasma glucose; HbA1c; diabetes duration; and retinal signs characteristic of diabetic retinopathy. For a first study specifically investigating hypertensive retinopathy, excluding known diabetes could substantially improve interpretability.

Smoking

Smoking can increase systemic inflammation and alter leukocyte counts. It can therefore influence NLR independently of hypertension. Smoking status should be categorized carefully, for example: never smoker; former smoker; current smoker. Where possible, pack-years should be calculated. Failure to account for smoking could produce a false association between NLR and retinal disease

Obesity

Obesity is another important confounder. Adipose tissue is metabolically active and can contribute to chronic low-grade inflammation. Obese individuals may therefore have elevated inflammatory markers even without overt infection. Body mass index and, ideally, waist circumference should be measured. This would allow researchers to determine whether the association between NLR and retinopathy remains after adjustment for adiposity.

Infection and Acute Inflammation

A simple but important issue is acute infection. A patient with malaria, respiratory infection, urinary tract infection or another acute inflammatory condition may have an elevated NLR. If such a patient is simultaneously hypertensive and has retinal changes, the NLR may reflect the infection rather than chronic vascular inflammation. Participants with active infection should therefore ideally be excluded. Alternatively, the presence of infection should be documented and incorporated into the statistical analysis. This consideration is particularly important in tropical settings.

Medications and NLR

Medication history should also be documented. Corticosteroids can alter circulating leukocyte profiles and may increase neutrophil counts while affecting lymphocyte distribution. Other medications may also influence inflammatory status. Antihypertensive drugs may potentially affect vascular inflammation indirectly through blood pressure control. The study should therefore record medication use rather than simply asking whether the participant is receiving treatment.

Age and Sex

Age is strongly associated with both hypertension and retinal vascular changes. Age may also influence leukocyte profiles and NLR.

Sex differences may likewise occur in immune function, hypertension patterns and retinal vascular

characteristics. Age and sex should therefore be included in all multivariable analyses.

Renal Function

Renal disease is particularly relevant because hypertension can cause kidney injury, while kidney disease can further worsen hypertension. Chronic kidney disease is also associated with systemic inflammation.

Therefore, patients with reduced renal function may have elevated NLR and more severe retinal disease simultaneously. A study that does not measure renal function may incorrectly interpret this relationship as a direct effect of NLR. At minimum, serum creatinine and estimated glomerular filtration rate should be measured. Urinary albumin-to-creatinine ratio would provide additional information where available.

Lipid Profile

Dyslipidaemia is associated with vascular disease and may contribute to retinal vascular abnormalities.

The study should ideally measure: total cholesterol; LDL cholesterol; HDL cholesterol; triglycerides.

Lipid-lowering treatment should also be documented. These variables can be included in multivariable models.

Complete Blood Count Beyond NLR

Although NLR is the principal variable, the complete blood count provides several other potentially useful indices.

The study should record: total white blood cell count; absolute neutrophil count; absolute lymphocyte count; monocyte count; hemoglobin; platelet count; mean platelet volume; red cell distribution width.

This permits calculation of additional inflammatory indices, if desired.

For example:

Platelet-to-lymphocyte ratio (PLR) and systemic immune-inflammation index (SII) may provide complementary information. However, adding too many biomarkers can dilute the central research question.

Relevance to Optometry

The study has particular relevance to optometric practice. Optometrists are often in a position to detect retinal vascular changes that may reflect systemic disease. A patient presenting for routine vision assessment may have retinal findings suggestive of longstanding hypertension. The discovery of moderate or severe hypertensive retinal changes should prompt appropriate systemic evaluation.

If NLR is found to correlate with retinal severity, it could potentially provide additional information about systemic inflammatory status. The optometrist could therefore become an important member of an interdisciplinary hypertension-management team.

Relevance to Haematology and Medical Laboratory Science

From the laboratory perspective, the study demonstrates how routine hematological parameters can be used to generate clinically meaningful indices. NLR is not a new laboratory test. It is a new way of interpreting familiar laboratory information. This is an important strength.

The medical laboratory scientist can contribute through: accurate differential leukocyte counts; quality assurance; NLR calculation; interpretation of abnormal leukocyte patterns; exclusion of obvious hematological confounders; and integration of laboratory findings with clinical data. This makes the project particularly suitable for a collaborative research team.

Proposed Conceptual Model

The proposed conceptual framework can be summarized as:

Hypertension



Persistent hemodynamic stress



Endothelial dysfunction



Oxidative stress



Immune and inflammatory activation



Neutrophil activation + lymphocyte alteration



Increased NLR



Systemic vascular inflammation



Retinal microvascular endothelial injury



Arteriolar narrowing / AV nicking



Retinal ischemia and vascular leakage



Haemorrhages / cotton-wool spots / exudates / oedema



Increasing hypertensive retinopathy severity

This model should be tested empirically rather than presented as an established causal pathway.

Conclusion

Hypertensive retinopathy is an important manifestation of systemic vascular injury. The retina provides a unique opportunity to observe microvascular consequences of hypertension directly, ranging from mild arteriolar narrowing to haemorrhages, cotton-wool spots, exudates, retinal oedema and optic disc swelling [2-4].

At the same time, hypertension is increasingly recognized as a disorder involving not only hemodynamic stress but also endothelial dysfunction, oxidative stress and immune-inflammatory activation. The neutrophil-to-lymphocyte ratio offers a simple way of capturing part of this inflammatory response. Evidence from systematic reviews and meta-analyses indicates that NLR is higher among hypertensive individuals and is associated with adverse cardiovascular outcomes [7,8,14]. Ophthalmic studies have similarly demonstrated elevated NLR in retinal artery occlusion and retinal vein occlusion, suggesting that systemic inflammatory status may be relevant to retinal vascular disease [9-12,19-23]. Nevertheless, there remains an important evidence gap concerning NLR and the severity of hypertensive retinopathy specifically. The existing literature does not justify claiming that an elevated NLR causes hypertensive retinopathy. Rather, the evidence supports a plausible hypothesis that systemic inflammation, reflected partly by an increased NLR, may be associated with the extent of retinal microvascular injury in patients with hypertension.

A well-designed Nigerian study could address this question by combining standardized blood-pressure measurement, complete blood count with differential, NLR calculation, assessment of major cardiovascular and inflammatory confounders, and objective retinal grading.

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Cite this article: Aloy-Amadi O.C., Enyereibe M.U, Nsonwu M.C. (2026). Neutrophil-To-Lymphocyte Ratio and Severity of Hypertensive Retinopathy: The Potential Role of Systemic Inflammation in Retinal Microvascular Injury. *Journal of Hematology Research and Blood Disorders*, BioRes Scientia Publishers. 2(1):1-10. DOI: 10.59657/3144-3419.brs.26.015

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Article History: Received: August 20, 2026 | Accepted: September 29, 2026 | Published: October 06, 2026