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ORIGINAL ARTICLE

Decreased neutrophil to lymphocyte ratio is associated with dengue with warning signs: A case-control study

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Abstract

Introduction: Because the clinical manifestations of dengue can range from mild to severe, finding methods to predict severe cases will be helpful in using medical resources efficiently. One potential predictor of severity is the neutrophil to lymphocyte ratio (NLR).
Material and method: We conducted a retrospective case-control study of 232 medical records from a hospital in northern Peru to evaluate how NLR may differentiate between cases of dengue with warning signs (DWWS) and cases without warning signs (DNWS).
Results: Bivariate analysis revealed that DWWS is associated with a decreased NLR, a history of reinfection, and younger age. The NLR distribution was biphasic for DNWS cases. We identified an NLR threshold of 1,5, which has a sensitivity of 86% for identifying DWWS cases and a specificity of 71% for correctly identifying DNWS cases.
Discussion: The biphasic NLR distribution suggests a single threshold is more effective for ruling DNWS out than for identifying cases. Nonetheless, these data suggest that NLR can serve to efficiently screen cases at high risk of developing DWWS and accurately rule out DNWS cases. NLR can be used as a simple diagnostic tool for triaging dengue patients, allowing for the optimized allocation of healthcare resources.

Keywords: dengue; neutrophil; lymphocyte

Disminución de la razón neutrófilo/linfocito se asocia con el dengue con signos de alarma: Un estudio de casos y controles

Resumen

Introducción: Dado que las manifestaciones clínicas del dengue pueden variar de leves a graves, encontrar métodos para predecir casos graves ayudará a optimizar el uso de los recursos médicos. Un posible predictor de gravedad es el índice neutrófilos-linfocitos (INL).
Material y método: Realizamos un estudio retrospectivo de casos y controles con 232 historias clínicas de un hospital del norte de Perú para evaluar cómo el INL puede diferenciar entre casos de dengue con signos de alarma (DWWS) y sin signos de alarma (DNWS).
Resultados: El análisis bivariado indicó que el DWWS está asociado con una reducción en el INL, la reinfección y la juventud. La distribución del INL fue bifásica en los casos de DNWS. Identificamos un umbral de INL de 1,5, que resulta en una sensibilidad del 86% para identificar casos de DWWS y una especificidad del 71% para identificar correctamente los casos de DNWS.
Discusión: La distribución bifásica del INL sugiere que un único umbral es más efectivo para descartar DNWS que para identificar casos. No obstante, estos datos indican que el INL puede servir para cribar de casos con alto riesgo de desarrollar DWWS y para descartar con precisión los casos de DNWS. El INL puede utilizarse como una herramienta diagnóstica simple para la clasificación de pacientes con dengue, lo que permite una asignación optimizada de los recursos sanitarios.

Palabras Clave: dengue; linfocito; neutrófilo

Introduction

Dengue is a vector-borne disease caused by any of the four genetically related but antigenically different viral serotypes. Infection with these viruses may be asymptomatic or cause mild disease that can be managed as an outpatient. However, in some cases, dengue infection can cause nausea, vomiting, rashes, leukopenia, as well as life-threatening hemorrhagic fever and hypovolemic shock[1–3]. To better categorize the clinical management of dengue, severity is classified into three groups: dengue without warning signs (DNWS), dengue with warning signs (DWWS), and severe dengue (SD). The latter two severities require monitoring in a hospital, whereas the first requires ambulatory monitoring[3,4].

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Recibido: 31/07/2025; Aceptado: 06/12/2025

Cómo citar este artículo: L.J. Fernández-Rodríguezo, *et al*. Decreased neutrophil to lymphocyte ratio is associated with dengue with warning signs: A case-control study. Infectio 2026; 30(1): 64-69

Dengue infection is increasing as human activity has increased the range of its vectors and spread dengue to all major tropical and subtropical regions of the world leaving about 40% of the world population at risk[1,3,5]. In 2023, more than 6 million cases and 6 892 deaths were reported. The infection rate has increased over the last five years[6]. This statistic likely underreports the actual prevalence due to poor health infrastructure and non-reporting of mild disease[1,6].

Because of the high prevalence of dengue, a large at-risk population, and the wide range of symptoms and disease progression dengue infection can cause, both understanding SD risk factors and developing sensitive and specific tests to predict how a patient will progress are helpful in making treatment efficient and allocating proper resources: knowing which patients will need increased surveillance can save lives. This need is especially acute in countries with limited healthcare infrastructure.

To date, risk factors such as being a child, previous dengue infection, and having diabetes or hypertension have been shown to be statistically associated with SD[1]. Furthermore, increased hematocrit with decreased platelet count, abdominal pain, lethargy, vomiting, hepatomegaly, ascites, pleural effusion, and melena have been established as warning signs associated with SD[7]. Other studies on blood parameters as severity predictors have shown promising results[8]. One promising and simple parameter is the neutrophil-to-lymphocyte ratio (NLR), which is a general measure of inflammatory status that has been studied in several disease states[9–11].

Given the potential usefulness of NLR in understanding other diseases, we decided to evaluate whether NLR was statistically associated with DWWS in a retrospective study of patients from Peru. Most studies on this subject have been conducted in Asia, which makes this study one of the few conducted in Latin America. Additionally, these worldwide studies have reported conflicting results[12–18]. We expected that DWWS would be associated with a decreased NLR, as dengue tends to provoke lymphocyte production, particularly after the first few days of infection.

Materials and methods

Study Design and Ethical Considerations

The study consisted of an evaluation of medical records of patients seen at Hospital I Florencia de Mora - EsSalud, Florencia de Mora, La Libertad, Peru (HFM), between March and May 2024. This was an observational retrospective case-control study. The study was approved by the Bioethics Committee of Antenor Orrego Private University, Trujillo, Peru, on June 18, 2024 (resolution number 01144-2024-UPAO). The review of medical records was conducted after the resolution approval date. The ethics committee determined that written informed consent was not necessary as the study was an analysis of medical records of routine care and the data were anonymized. The research was conducted in accordance with the Declaration of Helsinki 2008, especially regarding patient confidentiality[19].

Inclusion Criteria

Patient records were included in the study if there was evidence of a positive NS1/IgM rapid test for dengue, if the patient was older than 18 years of age at the time of medical consultation, and the record reported all variables analyzed in the study (age, sex, urban or rural address, previous dengue infection, detailed clinical presentation, and blood analysis upon examination). Dengue diagnosis was performed in accordance with the Peruvian Ministry of Health (MINSA) guidelines[20]. Records were excluded if they were incomplete, dengue was ruled out by additional laboratory tests, or there was evidence of one or more of the following: HIV infection, autoimmune disease, cancer, pregnancy, or coagulation disorders. Furthermore, each record was reviewed by an expert to ensure that both clinical findings and laboratory results were reasonable given the patient's status; irregularities in the report resulted in exclusion. These measures were taken to reduce bias in the clinical records included.

Defining DNWS and DWWS

Patient records were sorted as DWWS or DNWS according to the MINSA guidelines[20]. Patients with DWWS had to have at least one of the following: continuous intense abdominal pain or pain upon palpation of the abdomen; persistent vomiting; bleeding of the mucosa or skin of any type; lethargy, restlessness, or irritability; serous effusion, such as ascites; fainting; hepatomegaly; and/or progressive increase in hematocrit. Patients with DNWS did not have these signs but often had headaches, muscle aches, arthralgia, eye pain, and/or nausea.

Sample size

The sample consisted of 232 patients, 116 with DWWS (cases) and 116 with DNWS (controls). The sample size was determined using Epidat 4.3 and results from a published study[14].

Data Collection and Analysis

To analyze dengue-relevant information from the cases and controls, de-identified data on age, sex, whether the patient lived in a city, previous dengue infection, and NLR were collected. The NLR values used in this study reflect those first recorded during patient intake. Statistical calculations, including Fisher's exact test and Wilcoxon rank-sum test, were performed using R version 4.5.1. To determine the independent predictive value of the NLR in distinguishing DWWS from DNWS, multivariate binary logistic regression was performed. Disease severity (DWWS vs. DNWS) was the dependent variable. The regression included NLR, alongside age, sex (male vs. female), and reinfection status (yes vs. no). P values of less than 0.05 were considered significant.

The optimal threshold for differentiating between cases and controls was calculated using Receiver Operating Characteristic curve analysis and by maximizing the Youden Index (J = Sensitivity + Specificity -1), which balances the true positive and true negative rates.

Results

A total of 232 medical records of confirmed dengue cases seen between March and May 2024 at HFM were evaluated to search for associations between DWWS and the measured variables. All selected patients lived in a city. Table 1 summarizes the categorical variables of sex and previous dengue infection, sorted by cases and controls. Using Fisher's exact test, a significant positive association was observed between DWWS and previous dengue infection.

Table 2 summarizes the correlations between age and NLR in the cases and controls, as determined using the Wilcoxon rank-sum test. Both variables were statistically different between the cases and controls, with cases having a statistically significantly lower age and NLR. However, case and control data overlapped for both age and NLR. It is also worth mentioning that NLR values of the cases strongly clustered around 0,67 with a few outliers, while control NLR values tended to have a more bimodal distribution with peaks around 0,5 and 2,3 (Figure 1).

Table 3 presents the results of a binary logistic regression with dengue severity as the dependent variable and sex, history of previous infection, age, and NLR as the independent variables.

The results shown in Tables 1, 2, and 3 indicate that the NLR was negatively correlated with DWWS, with an odds ratio of approximately 0,4. This makes it possible to evaluate the NLR as a basis for a test for DWWS risk. It is also worth noting that applying Bonferroni corrections to the P values of multiple analyses does not increase any P threshold above the significance level.

To be a useful diagnostic test, the NLR threshold needs to be established. Although attempts have been made in the literature, no consensus exists on the normal and abnormal values for NLR[10–12,21]. For example, a suggested threshold of 0,8 would give a sensitivity of 62% and a specificity of 80%, which suggests a high correct rejection rate of true DNWS cases, but a comparatively low identification rate of true DWWS cases (Table 4). We used Receiver Operating Characteristic curve analysis to determine a threshold that maximized both sensitivity and selectivity. This analysis yielded a suggested threshold value of 1,5 with an area under the curve of 0,79, and a Youden Index of 0,569. This threshold captured 86% of actual DWWS cases and rejected 71% of DNWS cases (Table 4). A decrease in the NLR threshold would increase the test specificity at the expense of sensitivity[21].

Discussion

Dengue represents a challenge to health systems because some infections can result in life-threatening illness, while other cases have self-limiting, mild symptoms. Therefore, identifying high-risk patients can result in better individual treatment and better allocation of finite healthcare resources. To this end, we studied four easy-to-determine factors among dengue patients to determine whether these factors can be used to test DWWS.

NLR has emerged as an emerging marker in the diagnosis of various pathologies. The reduction of NLR in dengue may be associated with neutropenia induced by viral infection, which is known to cause neutrophil apoptosis and is an early indication of severe disease, usually preceding the clinical manifestation by several hours[10,22]. However, NLR does seem to rebound or fluctuate as the disease progresses[18,23,24].

We observed that a decrease in NLR was positively associated with DWWS, indicating that a low NLR is an indicator of more severe disease. Previously published reports frequently show significant differences in NLR between severe and non-severe cases, but the direction of the correlation is different, with some studies[12–14,17] concluding that a decrease in NLR is associated with severe disease, while others report the opposite[15,16]. From this study, it is becoming clear that when the NLR test is completed and how it changes during the course of infection is a likely stronger indicator of severity than a simple NLR test. Newly infected patients experience a decrease in NLR over the first week of infection, but this

Table 1. Sex and reinfection status of patients treated for dengue at HFM between March and May 2024

Variable	Dengue		Fisher Exact Test	
	DWWS (n = 116)	DNWS (n = 116)		
Sex			95% CI	P value
Female Male	71 (61,2%) 45 (38,8%)	59 (50,9%) 57 (49,1%)	0,875 – 2,656	0,146
Reinfection				
No	100 (86,2%)	114 (98,3%)	0,012 – 0,488	0,000853
Yes	16 (13,8%)	2 (1,7%)		

NLR: Neutrophil to lymphocyte ratio, DWWS: dengue with warning signs, DNWS: dengue without warning signs, CI: confidence interval, HFM: Hospital I Florencia de Mora – EsSalud

Table 2. Age and NLR of patients treated for dengue at HFM between March and May 2024

Variable	Dengue		Wilcoxon Rank Sum Test with continuity correction	
	DWWS (n = 116)	DNWS (n = 116)	U	P value
Age, y	Median: 37,5 IQR: 23,5	Median: 42,0 IQR: 23,0	8364,5	0,00137
NLR	Median: 0,755 IQR: 0,56	Median: 2,145 IQR: 1,835	10605	<0,001

NLR: Neutrophil to lymphocyte ratio, DWWS: dengue with warning signs, DNWS: dengue without warning signs, HFM: Hospital I Florencia de Mora - EsSalud

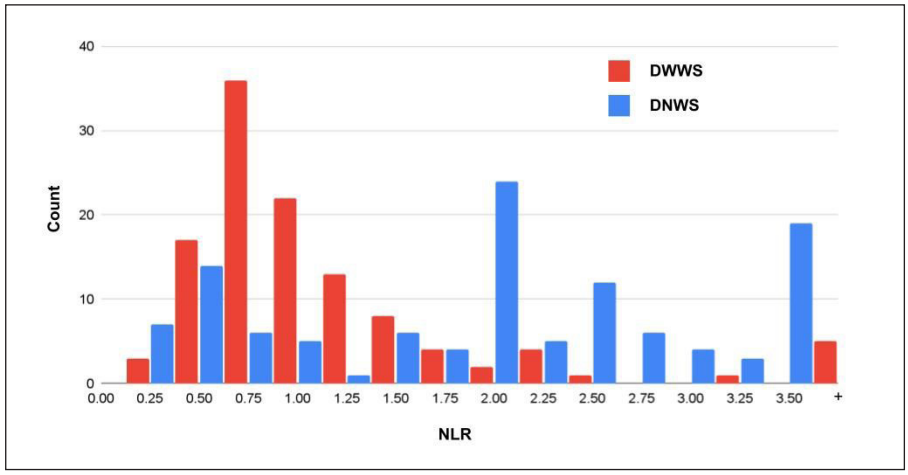

Figure 1. Histogram of NLR measurements separated by patients with DWWS (red) and those with DNWS (blue). Values >3,5 were added to the right bin.

parameter later rebounds, and evidence of a rebound is associated with recovery[18,23].

Although a universal clinical threshold value for NLR has not yet been established, its usefulness in predicting various diseases has been widely recognized [9]. In our study, two threshold values were evaluated: 1,5 as suggested by optimizing specificity and sensitivity, and 0,8 based on previous work to determine normal and pathological ranges [10,21]. Further evidence for a threshold value requires external validation using an independent cohort.

The NLR results determined here showed a biphasic pattern for DNWS patients but not for DWWS patients, which clustered towards low values of NLR only (Figure 1). Therefore, we observed that using NLR as a dengue severity test is sensitive in indicating DWWS patients (86% for a threshold of 1,5). However, the test is not very selective because of the overlap of values between patients with DNWS and DWWS, leaving several patients with DNWS with false positives (Figure 1). This means that NLR should not be used as a single diagnostic predictor for DWWS but rather as a helpful tool in evaluating dengue patients. Interestingly, this result is consistent with that of Navya et al., who showed a high specificity (94.4%) in identifying non-severe cases but a low sensitivity[14].

This finding presents an interesting question: whether those presenting with both low NLR and DNWS are different from those with high NLR DNWS. An analysis with a threshold NLR value of 1,5 indicated that females predominated in the low NLR DNWS group compared to the high NLR DNWS group (Fisher's Exact Test, p = 0,0135), while the ages of the groups were not significantly different (Wilcoxon Rank Sum Test W = 1393, p = 0,89). However, additional studies directly aimed at this observation are likely to provide more comprehensive results.

Age was another parameter that was significantly and negatively associated with the DWWS. These results are consistent with those of several previous studies[2,7]. Although some studies point to higher mortality in older adults due to decreased immune function, comorbidities, and the tropism of the virus by various organs, others suggest that the young continue to be the most affected by severe forms of the disease due to their greater vascular permeability[7,25,26].

Reinfection was also related to DWWS, and a history of dengue infection was positively associated with more severe symptoms. In this study, 13.8% of patients with warning signs had reinfection, which was significantly associated with an increased risk of severity (Tables 1 and 3). Similarly, Tsheten

Table 3. Multivariate binary logistic regression analysis using disease severity (DWWS as reference) as the dependent variable with NLR, age, sex (male as reference), and previous infection (yes as reference) as independent variables at HFM between March and May 2024.

	B	S. E.	Wald	p-value	Exp(B)	95% CI
NLR	-0,94	0,16	33,08	<0,001	0,39	0,28 – 0,54
Age	-0,03	0,01	7,34	0,007	0,97	0,96 – 0,99
Sex	-0,19	0,32	0,35	0,555	0,83	0,45 – 1,54
Reinfection	-2,33	0,92	6,43	0,011	0,10	0,011 – 0,46
Constant	4,83	1,03	21,85	<0,001	125,15	

NLR: Neutrophil to lymphocyte ratio, DWWS: dengue with warning signs, DNWS: dengue without warning signs, B: unstandardized beta coefficient, S.E.: standard error, Exp(B): exponentiated beta coefficient or odds ratio, CI: confidence interval, HFM: Hospital I Florencia de Mora - EsSalud

et al. in their systematic review and meta-analysis, found that secondary dengue infection was significantly associated with the development of severe disease[7]. This pathogenesis could be related to the antibody-dependent enhancement mechanism, in which pre-existing heterotypic antibodies bind to form immune complexes with virions without neutralizing them, thereby evading innate immunity[27]. In addition, during secondary infection, a robust immune response is developed by the early activation of cross-reactive T cells, which produce large amounts of proinflammatory cytokines and chemokines that promote inflammation and vascular leakage, contributing to disease severity[28]. These findings underscore the importance of preventive strategies to reduce the risk of reinfection and its clinical consequences.

In our sample, female patients predominated (61.2%). However, this proportion did not reach statistical significance when considering the gender ratio of the region where the study center was located (Fisher exact test, p=0.15)[29]. Regardless, this has been reported before, and there is some evidence that the greater proportion of females with dengue could be attributed to greater female exposure to vectors, given their domestic and diurnal behavior[23,30]. However, this hypothesis has been questioned by a study in Singapore by Yew et al., where they mention that no significant differences were found in terms of gender in recent dengue infection, despite the excess of male cases reported during the same year (p > 0.1)[31].

The major limitations of this study are that it had a small sample size, was conducted at a single center during a single outbreak, and considered the NLR of patients upon admission rather than controlling for the onset or evolution of the symptoms. Therefore, the generalizability of these findings to other populations with different genetic characteristics, other dengue serotypes, or other epidemiological contexts is limited. Thus, larger studies that include different populations and serotypes are necessary. Age, comorbidities, socioeconomic status, co-infection with other infectious diseases, and cultural differences could have also confounded the results. Therefore, follow-up work that includes monitoring both symptom severity and NLR over time might provide a more detailed view of how NLR can be used as a forward predictor of DWWS. In addition, future studies that include multiple clinics and a larger population may further confirm and validate the results and thresholds suggested here, have more generalizability, and provide the basis for more effective triage of dengue patients. Additional research questions worth exploring include elucidating the reasons for a low NLR without DWWS and determining the predictive value of NLR for severe dengue. Nonetheless, the NLR shows promise as a simple-to-measure statistic that can be used to eliminate cases of low concern, thereby decreasing the likelihood of overtreatment in mild dengue cases with a positive prognosis.

Table 4. Comparison of threshold values for NLR in cases and controls.

NLR	Dengue		Fisher exact test	
	DWWS (n = 116)	DNWS (n= 116)		
Threshold 0,8			95% CI	P value
High (> 0,8) Low (≤ 0,8)	44 72	93 23	0,080 – 0,283	<0,001
Threshold 1,5				
High (> 1,5) Low (≤ 1,5)	16 100	82 34	0,032 – 0,134	<0,001

NLR: Neutrophil to lymphocyte ratio, DWWS: dengue with warning signs, DNWS: dengue without warning signs, CI: confidence interval

Ethical considerations

Protection of Persons and Animals. Not applicable. No experiments on humans were done during this research, rather medical records explaining routine treatment were analyzed.

Protection of Vulnerable Populations. Not applicable. Vulnerable populations were not studied or experimented on during this research.

Confidentiality. Informed consent was not required as the bioethics committee of Antenor Orrego Private University has determined that it is not needed, as the study is based on clinical and laboratory data as part of routine care and that the presented data was anonymized.

Privacy. Given that confidentiality was respected, direct patient consent was deemed unnecessary for medical record review.

Financing. The study was self-funded by the authors.

Conflict of Interest Statement. The authors have no conflict of interest to declare.

Acknowledgements. The authors wish to thank the staff of Hospital I Florencia de Mora - EsSalud for providing access to the medical records necessary to complete this study.

Authors' contribution. Conceptualization: E.J.M.M., Data curation: E.J.M.M., V.H.B.Z. Formal analysis: V.H.B.Z. Investigation: E.J.M.M. Methodology: E.J.M.M. Supervision: L.J.F.R., V.H.B.Z. Writing: original draft: L.J.F.R., Writing: review and editing: L.J.F.R. All authors contributed to read and approved the version of the submitted manuscript.

References

1. Khan MB, Yang Z-S, Lin C-Y, et al. Dengue overview: An updated systemic review. J Infect Public Health 2023;16(10):1625–1642; doi: 10.1016/j.jiph.2023.08.001.
2. Harapan H, Michie A, Sasmono RT, et al. Dengue: A Minireview. Viruses 2020;12(8):829; doi: 10.3390/v12080829.
3. Wong JM, Adams LE, Durbin AP, et al. Dengue: A Growing Problem With New Interventions. Pediatrics 2022;149(6):e2021055522; doi: 10.1542/peds.2021-055522.

4. Pan American Health Association. Algorithms for the Clinical Management of Dengue Patients. Pan American Health Association. Pan American Health Association: Washington, DC; 2020.
5. Parveen S, Riaz Z, Saeed S, et al. Dengue hemorrhagic fever: a growing global menace. J Water Health 2023;21(11):1632–1650; doi: 10.2166/wh.2023.114.
6. Haider N, Hasan MN, Onyango J, et al. Global landmark: 2023 marks the worst year for dengue cases with millions infected and thousands of deaths reported. IJID Regions 2024;13:100459; doi: 10.1016/j.ijregi.2024.100459.
7. Tsheten T, Clements ACA, Gray DJ, et al. Clinical predictors of severe dengue: a systematic review and meta-analysis. Infectious Diseases of Poverty 2021;10(1):123; doi: 10.1186/s40249-021-00908-2.
8. Rafi A, Mousumi AN, Ahmed R, et al. Dengue epidemic in a non-endemic zone of Bangladesh: Clinical and laboratory profiles of patients. PLoS Negl Trop Dis 2020;14(10):e0008567; doi: 10.1371/journal.pntd.0008567.
9. Buonacera A, Stancanelli B, Colaci M, et al. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci 2022;23(7):3636; doi: 10.3390/ijms23073636.
10. Zahorec R. Neutrophil-to-lymphocyte ratio, past, present and future perspectives. Bratisl Lek Listy 2021;122(7):474–488; doi: 10.4149/BLL_2021_078.
11. Osuna-Ramos JF, Reyes-Ruiz JM, Ochoa-Ramírez LA, et al. The Usefulness of Peripheral Blood Cell Counts to Distinguish COVID-19 from Dengue during Acute Infection. Trop Med Infect Dis 2022;7(2):20; doi: 10.3390/tropicalmed7020020.
12. Prajapati AK. Significance of neutrophil to lymphocyte ratio evaluation as a prognostic indicator in dengue patients. World J Bio Pharm Health Sci 2024;18(3):009–017; doi: 10.30574/wjbphs.2024.18.3.0313.
13. Koundinya MA, Dasari D, Ashok S, et al. Neutrophil To Lymphocyte Ratio As Prognostic And Predictor Factor For Severity Of Dengue Fever - A Retrospective Observational Study In A Tertiary Care Centre. IAIM 2021.;8(12):46–52.
14. Navya P, Begum R, Thajudeen AS, et al. Navigating the Haematological Maze: Unraveling the Role of NLR and PLR as Predictors of Dengue Severity- A Cross-sectional Study from Southern India. JCDR 2024;18(2):EC23–EC26; doi: 10.7860/JCDR/2024/68904.19162.
15. Wazib A, Rahman S, Mamun KAA, et al. Predicting the Risk of Dengue Shock Syndrome with Neutrophil-Lymphocyte Ratio on the Third Day of Dengue Infection. East West Medical College Journal 2025;13(1):50–53; doi: 10.3329/ewmcj.v13i1.77625.
16. Agrawal S, Kumar S, Talwar D, et al. Significance of Neutrophil-lymphocyte Ratio, Neutrophil-platelet Ratio, and Neutrophil-tolymphocyte and Platelet Ratio in Predicting Outcomes in Dengue Patients on Admission in Wardha, Maharashtra, India: A Retrospective Cohort Study. JCDR 2023;17(11):OC01–OC04; doi: 10.7860/JCDR/2023/65292.18658.
17. Yuditya DC, Sudirgo I. The Relation between Neutrophil Lymphocyte Count Ratio (NLCR) and Dengue Infection Grade of Severity in Adult Patients in RS Muhammadiyah Ahmad Dahlan Kediri in January 2019. STRADA : Jurnal Ilmiah Kesehatan 2020;9(1):20–25; doi: 10.30994/sjik.v9i1.265.
18. Pribadi MI, Umma HA, Siregar R. Neutrophil-lymphocyte ratio as an indicator of recovery phase in children with dengue fever. Trends in Pediatrics 2025;6(1):25–32; doi: 10.59213/TP.2025.199.
19. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310(20):2191–2194; doi: 10.1001/jama.2013.281053.
20. Ministerio de Salud. Resolución Ministerial N.° 175-2024-MINSA. 2024. Available from:https://www.gob.pe/institucion/minsa/normaslegales/5323501-175-2024-minsa [Last accessed: 11/7/2025].
21. Forget P, Khalifa C, Defour J-P, et al. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Research Notes 2017;10(1):12; doi: 10.1186/s13104-016-2335-5.
22. Galani IE, Andreakos E. Neutrophils in viral infections: Current concepts and caveats. J Leukoc Biol 2015;98(4):557–564; doi: 10.1189/jlb.4VMR1114-555R.
23. Böer LM, Junqueira IC, Nascimento TC do, et al. Monocyte-lymphocyte, neutrophil-lymphocyte, and platelet-lymphocyte ratios as inflammatory biomarkers of clinical dengue severity. Bioscience Journal 2024;40:e40038; doi: 10.14393/BJ-v40n0a2024-67413.
24. Ishaque N, Siddique MU, Imran A, et al. Utilization of Neutrophil to Lymphocyte Ratio to Assess Recovery in Patients with Dengue. Journal of Haematology and Stem Cell Research 2022;2(2):77–80.
25. Rosso F, Parra-Lara LG, Agudelo-Rojas OL, et al. Differentiating Dengue from COVID-19: Comparison of Cases in Colombia. Am J Trop Med Hyg 2021;105(3):745–750; doi: 10.4269/ajtmh.20-0912.
26. Pang J, Hsu JP, Yeo TW, et al. Diabetes, cardiac disorders and asthma as risk factors for severe organ involvement among adult dengue patients: A matched case-control study. Sci Rep 2017;7:39872; doi: 10.1038/srep39872.
27. Narayan R, Tripathi S. Intrinsic ADE: The Dark Side of Antibody Dependent Enhancement During Dengue Infection. Front Cell Infect Microbiol 2020;10:580096; doi: 10.3389/fcimb.2020.580096.
28. Khanam A, Gutiérrez-Barbosa H, Lyke KE, et al. Immune-Mediated Pathogenesis in Dengue Virus Infection. Viruses 2022;14(11):2575; doi: 10.3390/v14112575.
29. Instituto Nacional de Estadística e Informática. La Libertad Compendio Estadístico 2023. Instituto Nacional de Estadística e Informática: Lima, Peru; 2023.
30. García-Vilca L, Cabanillas Mejía EA, Valderrama Valdivia C, et al. Factores de riesgo para dengue con signos de alarma en el servicio de emergencia de un hospital público. Un estudio caso control. Acta Médica Peruana 2024;41(2):83–91; doi: 10.35663/amp.2024.412.2833.
31. Yew YW, Ye T, Ang LW, et al. Seroepidemiology of dengue virus infection among adults in Singapore. Ann Acad Med Singap 2009;38(8):667–675.