

International Journal of Pediatrics and Neonatology

ISSN Print: 2664-8350
ISSN Online: 2664-8369
Impact Factor: RJIF 5.26
IJPN 2024; 6(2): 74-76
www.pediatricsjournal.net
Received: 06-05-2024
Accepted: 08-06-2024

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Absolute neutrophil counts and neutrophil to lymphocyte ratio as predictive markers of dengue severity among children

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DOI: <https://doi.org/10.33545/26648350.2024.v6.i2b.84>

Abstract

Introduction: Dengue fever is known to have an unpredictable course and outcome. Because of this uncertainty, predictive markers are needed for early detection and prognosis of severe dengue. Studies on the correlation of degrees of Neutropenia and Neutrophil-Lymphocyte Ratio (NLR) with dengue severity on the pediatric population are scarce, and its clinical significance is still uncertain.

Objective: To determine the correlation of Absolute Neutrophil Counts (ANC) and Neutrophil-Lymphocyte Ratio (NLR) during the acute phase of dengue infection with the development of severe dengue among children aged 0-18 years.

Methodology: This is a retrospective descriptive correlational study. The case details of children aged 0-18 years with laboratory-confirmed dengue who were admitted to SIMS&RC from August 1, 2023 to January 31, 2024 were reviewed. Data collection was done. Data were analyzed. Statistical tests were used to determine the association of ANC and NLR with dengue severity.

Results: Out of 112 eligible children, 100 subjects were enrolled. Abnormal ANC was noted in 52% of subjects where, 24% had mild neutropenia, 18% had moderate neutropenia and 10% had severe neutropenia. Almost 42% of subjects had high NLR. There was no significant association noted between ANC and dengue severity. However, with increasing severity of neutropenia, risk for severe dengue also increased. No significant association was also noted between NLR and dengue severity.

Conclusions: There is no significant correlation between neutropenia during the febrile phase of dengue infection with the development of severe dengue in paediatric patients. However, a trend towards increasing risk for developing severe dengue was noted, with increasing severity of neutropenia. High NLR during the febrile stage of dengue, likewise, is not significantly associated with progression to severe disease.

Keywords: Absolute neutrophil count, neutrophil lymphocyte ratio, paediatrics, dengue

Introduction

Dengue is an arboviral disease caused by flavivirus. It has four serotypes: DENV-1, DENV-2, DENV-3, and DENV-4. It is a single stranded, non-segmented RNA virus, belongs to genus flavivirus, family Flaviviridae. In recent years, dengue has become one of the most significant and fast emerging tropical viral diseases. Dengue has a broad clinical manifestation, ranging from non-specific febrile illness, dengue fever (DF) with and without warning signs and severe dengue, according to 2009 WHO revised classification.

Early recognition of dengue is mostly challenging as, the initial symptoms are often non-specific, viremia may be below detectable levels and serological confirmation in dengue is late in the course of illness. There are no accepted clinical guidelines for early recognition of dengue infection and no consensus to whether clinical features to distinguish dengue from other febrile illness also. Most patients recover from a non-severe clinical course while some progress to severe disease. It is therefore prudent to develop diagnostic tools for early detection of impending severe dengue disease.

As Dengue fever is known to be a non-inflammatory type of disease, inflammatory biomarkers such as Neutrophil-Lymphocyte Ratio (NLR) is not expected to rise in dengue fever. Also, one of the features of dengue virus is its ability to suppress bone marrow production of leukocytes specifically neutrophils leading to absolute neutropenia.

Recent researches have utilized absolute neutrophil count (ANC) as an early indicator of severe dengue. However, these studies warrant further validation in other regions and age groups [1-4].

To fill this lacuna, this study will utilize ANC and NLR as early predictive markers of dengue severity in an attempt to establish a correlation between the degree of neutropenia and high NLR to the development of severe dengue infection in the pediatric population.

Materials and Methods

Objectives

To determine the correlation of Absolute Neutrophil Counts (ANC) and Neutrophil-Lymphocyte Ratio (NLR) during the acute phase of dengue infection with the development of severe dengue among children aged <18 years.

Study design: Retrospective descriptive correlational study

Place of study: Saphthagiri institute of medical sciences and research center.

Study period: 6 months (August 2023 to January 2024)

Sample size: 100

Inclusion criteria:

All children who were admitted to SIMS & RC, aged <18 years, with laboratory-confirmed dengue fever.

Exclusion criteria

1. Conditions which involve an inflammatory process and/or tissue damage that can cause high NLR ratio, including, but not limited to: Diagnosed concomitant bacterial infection upon admission, known malignancy, known autoimmune diseases, burns, trauma, known cardiovascular diseases.
2. Other conditions that can induce neutropenia by themselves, including, but not limited to: Diseases of the bone marrow (leukemias, myelodysplastic syndrome, aplastic anemia, myelofibrosis), Congenital disorders of bone marrow function, Hypersplenism, Autoimmune diseases, Intake/administration of chemotherapeutic drugs.

Methodology

The study was conducted in children, meeting inclusion criteria, admitted in SIMS & RC. Each child's demographics were collected. ANC and NLR ratio on admission, and on what day from illness onset the CBC was taken, were noted. ANCs were tabulated and stratified as Normal ANC, Mild Neutropenia, Moderate Neutropenia and Severe Neutropenia. NLRs were stratified as Normal NLR and High NLR. The number of patients with severe dengue as final diagnosis were noted. All data and results were noted, tabulated and processed for statistical analysis.

Statistical analysis

All collected data were tabulated. Descriptive statistics were applied to analyze the gathered information. Categorical variables were described using frequency and percentage, while continuous variables were summarized using the median and standard deviation. The Chi-square test was employed to assess the association between ANC, NLR, and dengue severity. The relative risk, along with its 95% confidence interval, was calculated to determine the strength of this association. Analysis was performed using IBM SPSS Statistics version 20.0.

Results

There were 112 pediatric dengue cases admitted to our Hospital from August, 2023 to January 2024. 100 patients aged <18 years, with laboratory-confirmed dengue fever, within the first 72 hours of illness onset were enrolled in the study.

Age ranged from 6 months – 16 years with a mean of 8.3 years (Table 1). There were more males than females with 62% and 38%, respectively (Graph 1).

Table 1: Distribution based on age

| Age | Frequency (%) |
|-------------|---------------|
| 0-3 months | 0 |
| 4-11 months | 2 (2) |
| 1-3 years | 12 (12) |
| 4-10 years | 58 (58) |
| 11-14 years | 22 (22) |
| 15-18 years | 6 (6) |

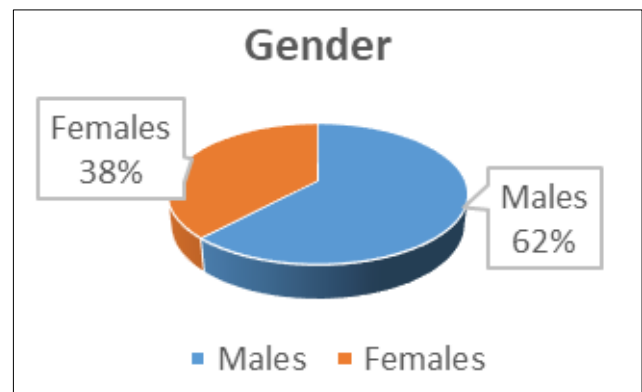


Fig 1: Distribution based on Gender

Table 2 and 3 depict the distribution of subjects according to laboratory parameters. Abnormal ANC was noted in 52 (52%) of subjects where, 24 (24%) had mild neutropenia, 18 (18%) had moderate neutropenia and 10 (10%) had severe neutropenia. Almost 42% of subjects had high NLR.

Table 2: Distribution based on absolute neutrophil count (ANC)

| Absolute Neutrophil Count (ANC) [5] | Frequency (%) |
|-------------------------------------|---------------|
| Normal ANC (>1500) | 48 (48) |
| Mild neutropenia (1000-1500) | 24 (24) |
| Moderate neutropenia (500-1000) | 18 (18) |
| Severe neutropenia (<500) | 10 (10) |

Table 3: Distribution based on Neutrophil-Lymphocyte Ratio (NLR)

| Neutrophil-Lymphocyte Ratio (NLR) [6] | Frequency (%) |
|---------------------------------------|---------------|
| Normal NLR | 58 (58) |
| High NLR | 42 (42) |

Table 4: Severity of Dengue in the study population

| Severity of Dengue [7] | Frequency (%) |
|------------------------------------|---------------|
| Dengue fever without warning signs | 30 (30) |
| Dengue fever with warning signs | 52 (52) |
| Severe Dengue | 18 (18) |

Out of 50 children with laboratory-confirmed dengue fever, 9 (18%) were found to have severe dengue, 26 (52%) were found to have dengue with warning signs and 15 (30%) dengue without warning signs (Table 4).

Based on the results of the study, there was no significant association noted between ANC and dengue severity as shown by all p values > 0.05 . However, a trend towards increasing risk for severe dengue was noted with increasing severity of neutropenia. The results also showed no significant association noted between NLR and dengue severity ($p>0.05$).

Discussion

Majority of the patients with dengue were between 4 to 10 years old which is similar to a study done in a tertiary hospital in Eastern India in 2019 where most of the dengue-afflicted patients involved also belong to the 4-10 years old age group⁸. Incidence distribution is higher in males which accounted for 62% of the patients involved in the study. This is in correlation with the report from WHO from January 1 to March 29, 2008 which showed that majority of dengue cases were males^[9].

Most cases had non-severe dengue (82%) and only 18% developed severe dengue during their hospitalization. This result is comparable to the studies done in India by Purkait and Basu where only 12.73% of the cases included had severe dengue^[8].

Bone marrow suppression is a recognized hallmark of dengue fever, impacting all cell populations within the bone marrow. Although neutropenia is less commonly reported in dengue infections, studies determining the correlation between neutropenia and dengue severity are scarce in both pediatric and adult populations.

In our study, neutropenia was present in 52% of the subjects involved. However, neutropenia in our study was not significantly associated with the development of severe dengue. This supports the findings from a study done by Khandelwal R. and Khandelwal L.M. on correlation of ANC and dengue severity^[3]. Despite the absence of significant association of ANC and dengue severity in our study, it is important to note that the results revealed a trend towards increasing risk for developing severe dengue as the severity of neutropenia increases.

There is no significant association between high NLR during the febrile phase of dengue and progression to severe disease. This is in concordance to results shown in a study done by Karla *et al.* where NLR was used as one of the prognosticators of severe dengue^[10].

Conclusion

No significant correlation exists between neutropenia during the febrile phase of dengue infection and the development of severe dengue in children. However, a trend was observed indicating an increased risk of severe dengue with greater severity of neutropenia. Similarly, a high NLR during the febrile stage of dengue (the first 72 hours) is not significantly associated with progression to severe disease.

Acknowledgments

I take this opportunity to extend my gratitude to all those who helped and guided me to complete this study.

Funding

No funding sources

References

1. Prayon KM, Oncog AS. Absolute neutrophil counts and neutrophil to lymphocyte ratio as early predictive markers of dengue severity among children admitted in

Governor Celestino Gallares Memorial Hospital: A 5-year retrospective study. *Acta Sci Paediatr.* 2022;5(7):37-45.

2. Atukuri SR, Nayak P. Correlation of C-reactive protein and neutrophil counts as early indicators of severe dengue in children. *Int J Contemp Pediatr.* 2017;4(2):450-4.
3. Khandelwal R, Khandelwal LM. Effect of dengue fever on the total leucocyte count and neutrophil count in children in early febrile period. *Int J Pediatr Res.* 2017;4(10):617-22.
4. Chadwick D, Arch B, Wilder-Smith A, Paton N. Distinguishing dengue fever from other infections on the basis of simple clinical and laboratory features: Application of logistic regression analysis. *J Clin Virol.* 2006;35(2):147-53.
5. Beers MH, Berkow R. *The Merck Manual of Diagnosis and Therapy.* Merck Research Laboratories; 1999.
6. Dursun A, Demirci H, Yigit M, Kelekci S. Neutrophil-to-lymphocyte ratio and mean platelet volume can be useful markers to predict sepsis in children. *Pak J Med Sci.* 2018;34(4):918-22.
7. Halstead SB. *Dengue Fever and Dengue Hemorrhagic Fever.* In: Kliegman RM, Stanton BF, St Geme JW, Schor NF, editors. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia: Elsevier; 2016. p. 1629.
8. Purkait R, Basu R. The changing clinico-demographic profile of dengue infection in children: A hospital-based study from Eastern India. *Int J Community Med Public Health.* 2020;7(5):1901-6.
9. World Health Organization. *Western Pacific, country health information profiles. Revision.* Geneva: World Health Organization; 2009.
10. Nusa K, Sugiarto S, Fathoni A, Widodo B, Bahar E. Hubungan ratio neutrophil dan limfosit pada penderita infeksi virus dengue. *Jurnal e-Clinic (eCI).* 2015;3(1).

How to Cite This Article

Deshapande VB, Dinakara N, Somashekar C, Kartheeka MG, Revanna R Meda P. Absolute neutrophil counts and neutrophil to lymphocyte ratio as predictive markers of dengue severity among children. *International Journal of Pediatrics and Neonatology.* 2024;6(2):74-76.

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