



PREDICTING THE RISK OF DENGUE SHOCK SYNDROME WITH NEUTROPHIL-LYMPHOCYTE RATIO ON THE THIRD DAY OF DENGUE INFECTION

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Article history:

Received: 4 November 2024

Accepted: 1 December 2024

Abstract:

Background: Dengue is an endemic infection in Bangladesh with frequent outbreaks. Dengue shock syndrome (DSS) contributes to the majority of mortality in dengue infection. Neutrophil-lymphocyte ratio (NLR) was found as a predictor of severe dengue in a recent study.

Objective: This study was conducted to assess the association of NLR and the development of DSS.

Methods: This case-control study was conducted on 42 dengue patients admitted under the Department of Medicine of Shaheed Monsur Ali Medical College Hospital from July to October 2023. Association of NLR on the third day of fever with DSS was assessed following appropriate statistical procedures.

Results: Mean NLR on the third day of fever was higher in DSS patients. NLR 2 or more was associated with a statistically significant higher proportion of DSS.

Conclusion: An NLR 2 or more on the third day of fever possesses a higher risk of developing DSS.

Keywords:

Dengue shock syndrome, neutrophil-lymphocyte ratio.

EWM CJ Vol. 13, No. 1, January 2025: 50-53

Introduction

Dengue is an endemic infection in Bangladesh with frequent outbreaks. The majority of the outbreaks occurred during the months of July to November comprising 82% cases since 2008¹. The 2023 dengue outbreak is the biggest one in Bangladesh with 2,77,801 cases and 1393 deaths (mortality rate 0.5%)².

The major cause of death in dengue infection is dengue shock syndrome (DSS)³. Total count of WBC <5,000/

cu mm and platelet <1,00,000/cu mm are regarded as high risk of dengue haemorrhagic fever (DHF) and subsequent DSS³.

Recent studies have identified neutrophil-lymphocyte ratio (NLR) as a predictor of severe dengue. Both high and low NLR were found to be associated with adverse outcomes in different studies³⁻⁷. There is no published study in Bangladesh on the prognostic value of NLR in the development of DSS.

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Objective

This study was aimed at finding the association between NLR and DSS in dengue infection.

Methods

This case-control study was conducted on the dengue patients admitted under the Department of Medicine of Shaheed Monsur Ali Medical College Hospital from July to October 2023. Data were collected from the patient records of the hospital. Confirmed cases of dengue fever with positive NS1 antigen and/or Anti-Dengue IgM tests, aged >12 years, whose complete blood count (CBC) on day three of fever was available, were included as study participants. Dengue patients with co-infection, pregnancy or co-morbidities like ischaemic heart disease, heart failure, chronic kidney disease, chronic liver disease and systemic lupus erythematosus were also excluded.

DSS was defined as any of: 1. narrow pulse pressure (<20 mmHg), 2. systolic blood pressure (SBP) <90 mmHg and/or diastolic blood pressure (DBP) <60 mmHg with low volume pulse and/or cold extremities and 3. unrecordable blood pressure⁸. The DSS patients with recordable and unrecordable blood pressure were designated as compensated shock and profound shock, respectively⁸. Thirty DSS patients were randomly selected as cases initially. Nine were removed subsequently due to inconsistent data. Equal number of age and gender-matched dengue patients who did not develop DSS were taken as controls.

The neutrophil-lymphocyte ratio was calculated from the CBC on day three of fever. The third day was chosen because majority of the patients presented on third day or later, and CBC on first two days were not available. The NLR between the DSS patients and controls were compared quantitatively with Mann-Whitney *U* test as the data were skewed. The association of NLR and DSS was assessed with odds ratio (OR) and Chi-square test. A *p*-value of <0.05 was considered statistically significant in all the comparisons. Statistical Package for the Social Sciences (SPSS) version 25.0 and Microsoft Excel were used for statistical analyses.

Ethical consideration

The study was conducted with the formal approval of the Institutional Ethical Review Board (IERB) of Shaheed Monsur Ali Medical College Hospital (Ref: SMAMC/04/2023/1789, dated 04/10/2023). Informed written consent was taken from every study participant.

Results

Total 42 study participants were included in the study – 21 DSS patients and 21 dengue patients who did not develop DSS as controls. Among 21 DSS patients, 19 (90.5%) had compensated shock and 2 (9.5%) had profound shock. Both the DSS and the control groups had 12 males and 9 females. The mean age was 31.6±2.6 years (range 13-50 years) in the DSS group and 31.1±2.4 years (range 13-50 years) in the control group. The majority of the study participants (64%) were within 21-40 years age group in both DSS (62%) and controls (67%). There was no statistically significant difference in ages between the two groups (*p*-value 0.9).

The total count (TC) of white blood cell (WBC) was 1700-8300/cu mm, with a median and inter-quartile range (IQR) of 3400/cu mm and 2800-5400/cu mm in the DSS group. Median and IQR of total WBC count were 3700/cu mm and 2850-4600/cu mm in the control group. No statistically significant difference in total WBC count was found between the two groups (*p*-value 0.9). (Figure-1, Table-I)

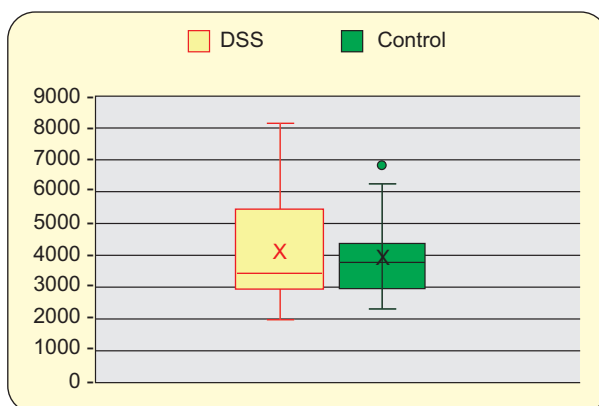


Figure 1: Total WBC count in DSS and control groups

Table-I
WBC total count and NLR in DSS and control groups

Parameter	DSS	CON	p-value
WBC TC ¹	3400	3700	0.9 ²
/cu mm	(2800-5400)	(2850-4600)	
NLR ¹	2.5	1.4	0.007 ²
	(1.7-3.0)	(0.8-2.0)	

CON-control 1-Median (IQR)

2-Mann-Whitney *U* test

Median and IQR of NLR were 2.5 and 1.7-3.0 in the DSS group. In the control group, median and IQR of NLR were 1.4 and 0.8-2.0. NLR was higher in DSS group, which was statistically significant (p-value 0.007). (**Figure-2, Table-I**)

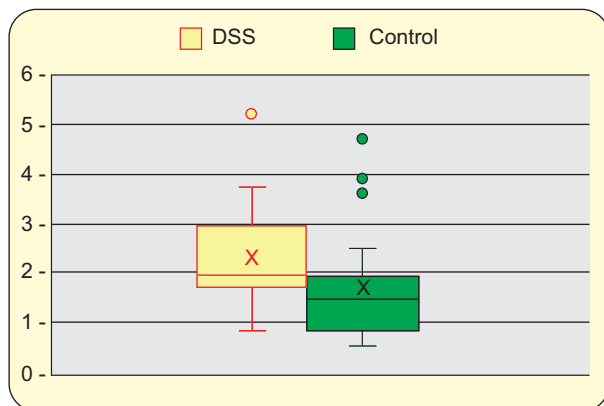


Figure 2: NLR in DSS and control groups

The proportion of study subjects with $\text{NLR} \geq 2$ was compared between the two groups as this value was assessed in a recent study on the South Asian population⁷. In the DSS group, 16 (76%) had an $\text{NLR} \geq 2$, while 5 (24%) had an $\text{NLR} < 2$. The number of $\text{NLR} \geq 2$ and $\text{NLR} < 2$ among the controls were 5(24%) and 16(76%), respectively. $\text{NLR} \geq 2$ was associated with a higher proportion of DSS than those with an $\text{NLR} < 2$, with an odds ratio of 10.2 (95% confidence interval 2.5-42.4), which was statistically significant (p-value 0.002). (Table-II)

Table-II
Association of NLR and DSS.

NLR	DSS	CON	OR	95% CI	p-value
≥ 2	16(76)	5(24)	10.2	2.5-42.4	0.002 ¹
< 2	5(24)	16(76)			

CON-Control; OR-Odds ratio

CI-confidence interval

1-Chi-square test with Yate's Correction

Percentages are given within the parentheses

Discussion

This case-control study was conducted on hospital-admitted dengue patients of both genders, covering a wide range of ages. The study participants were 58% males and 42% females with 64% within 21-40 years age group. Mahmood et al found similar gender and age distribution in a study on dengue fever in Dhaka⁹.

The mean total count of WBC was similar to that found in Sri Lanka¹⁰. There are contradictory results among different studies on the prognostic value of NLR in dengue infection. Few recent studies found a high NLR associated with better outcomes in dengue infection³⁻⁶. However, Ishaque et al. concluded a higher $\text{NLR} (\geq 2)$ on day three of dengue infection as a predictor of severe dengue⁷. The mean NLR on the third day was significantly higher in DSS patients than in the controls. $\text{NLR} \geq 2$ was associated with a higher proportion of DSS in the study subjects. These results were consistent with the findings of Ishaque et al⁷.

Limitation & Recommendation

This was a single-centre case-control study on a small number of participants. A multi-centre prospective study with a large sample size is recommended to assess the predictive value of NLR in the development of DSS.

Conclusion

A higher neutrophil-lymphocyte ratio on the third day of fever was observed in DSS patients. An $\text{NLR} \geq 2$ on the third day of dengue infection possesses a higher risk of developing DSS. Dengue infection with $\text{NLR} \geq 2$ on the third day of fever should be monitored closely and better be discharged after complete recovery.

Author contribution

Amit Wazib - conceptualized the study, literature review, study protocol and study design. Shaila Rahman - data analysis. Kazi Abdullah Al Mamun – Critical review. Md. Rayhan Ahmed, Safwanul Aman, MD Asaduzzaman Babu, Ahnaf Tahmid, Tasfia Hossain Nishat and Israt Jahan Ira - data collection.

Budget and funding

The study was conducted within a small budget arranged by the authors, and did not receive any research grant.

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