RESEARCH ARTICLE

NEUTROPHIL-LYMPHOCYTE RATIO AS A PROGNOSTIC INDICATOR IN DENGUE FEVER PATIENTS AT TERTIARY CARE HOSPITAL IN NORTHWEST-MAHARASHTRA

Dr. Anirudha Sadgir[1], Dr. Khushal Durge[2] and Dr. Satish Masavkar[3]

1. Junior Resident, Department of General Medicine, SMBT IMS & RC, Dhamangaon, Igatpuri, Nashik, Maharashtra.
2. Junior Resident, Department of General Medicine, SMBT IMS & RC, Dhamangaon, Igatpuri, Nashik, Maharashtra.
3. Professor and HOU, Department of General Medicine, SMBT IMS & RC, Dhamangaon, Igatpuri, Nashik, Maharashtra.

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Manuscript Info	*Abstract*
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Introduction- Dengue is regarded as the most important arthropod-borne viral infection in humans and is the second most important re-emerging tropical disease. Dengue infections are increasing resulting in more illness and death and in 2012 World Health Organization (WHO) reclassified dengue as the most important mosquito-borne viral disease in the world. Given the heterogeneous nature of the clinical presentation of dengue, identifying robust and sensitive clinical or laboratory predictors of dengue fever and its severity has not been an easy task. Neutrophil-to-lymphocyte ratio (NLR) can be easily calculated based on a complete blood count by dividing the Neutrophil percentage by Lymphocyte percentage. There is enough literature to suggest that NLR has prognostic significance in various diseases. However, no studies have focussed on NLR as a prognostic marker for dengue.

Aim- To study NLR in dengue patients and assess its role in relation with age, gender,serological tests for dengue and platelet count.

Materials and Methods- This retrospective observational study was carried out at Tertiary care hospital in Northwest Maharashtra. 100 diagnosed and admitted cases of dengue were included in this study. Clinical data and laboratory data were reviewed and analysed. Chi Square test was done and its significance noted.

Results- In our study, Ns1Ag dengue serology test was found to be more common in males indicating recent infection and Ns1Ag, IgM and IgG more common in females indicating recent and past infection. NLR < 2 strongly correlates with low platelets indicating severity of disease and reversal of NLR > 2 correlates with improvement of disease. NLR < 2 was more common in 0-20 years age group, younger the age lesser the NLR and hence more severe the disease.

Conclusion- From our study we found that there is a significant relation between NLR to the severity of dengue fever in adult patients and by keeping an eye on the NLR we can predict the prognosis and the severity of the disease in patient. Lower the NLR ratio severe the

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Corresponding Author:- Dr. Anirudha Sadgir
Address:- Junior Resident, Department of General Medicine, SMBT IMS & RC, Dhamangaon, Igatpuri, Nashik, Maharashtra.

disease. Hence NLR can be used as a prognostic indicator in dengue patients.

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Introduction:-

1. Dengue is regarded as the most important arthropod-borne viral infection in humans and is the second most important re-emerging tropical disease.[1] Dengue Virus (DENV) is a mosquito-borne single-stranded RNA virus belonging to the family Flaviviridae.[2]
2. Human transmission occurs from bites of infected mosquitoes, viz. Aedes aegypti (A. aegypti) and Aedes albopticus (A. albopticus).[2] Antigenically, there are four dengue serotypes identified as DENV1, DENV2, DENV3 and DENV4 that are endemic throughout the tropical and subtropical regions of the world.[3]
3. Dengue infections are increasing resulting in more illness and death and, in 2012 World Health Organization (WHO) reclassified dengue as the most important mosquito-borne viral disease in the world.[4,5]
4. Given the heterogeneous nature of the clinical presentation of dengue, identifying robust and sensitive clinical or laboratory predictors of dengue fever and its severity has not been an easy task.
5. Neutrophil-to-lymphocyte ratio (NLR) can be easily calculated based on a complete blood count by dividing the Neutrophil percentage by Lymphocyte percentage.
6. There is enough literature to suggest that NLR has prognostic significance in various diseases. However, no studies have focussed on NLR as a prognostic marker for dengue.
7. This study aims to look into the possibility of NLR as an easily accessible marker for the prognostication of dengue fever.

Materials And Methods:-

1. This retrospective record-based study was carried out at SMBT IMS & RC, Dhamangaon, Ghoti, Igatpuri, Nashik. 100 diagnosed cases of dengue were included in this study.
2. The statistical analysis was done on Microsoft Excel and P value or Chi Square test was done and its significance noted.
3. After routine informed consent from patient, 2ml venous blood was collected from antecubital vein under aseptic precautions in a EDTA bulb.
4. Smears were examined by pathologist and hematologic parameters with special emphasis on WBC differentials and platelet count were reconfirmed on microscopy.
5. Dengue serology was performed by Rapid test Immunochromatographic testing and confirmed by ELISA.

Aim
To study neutrophil lymphocyte ratio in dengue cases and assess its role in relation with various demographic, serologic parameters and platelet count.

Inclusion Criteria
All cases above 16 years of age diagnosed as Dengue positive (Ns1Ag or IgM or IgG or a combination of these) during the period June 2021 to October 2022 were included.

Exclusion Criteria
All other seronegative viral infections were excluded.

Results:-
Total of 100 cases of dengue, admitted to the hospital from June 2021- Oct 2022 were studied.

Table-1 revealed that males were predominantly affected. Primary Dengue infection (NS1+IgM) was more dominant in males. However, secondary dengue (NS1+IgM+IgG) was more common in females.

Table 1:- Demography of Dengue patients.

CASE STUDY	NLR<2	NLR>2	TOTAL	P value = 0.244
NS1Ag	40	13	53	(not significant)
NS1Ag, IgM	5	5	10	

NS1Ag, IgG, IgM	4	1	5	
IgG	16	2	18	
IgM	11	3	14	

In Table-2, It was noted that predominant age group affected was in 23 – 28 years, followed by 29 – 34 years, suggesting that outdoor activity made people prone to dengue.

Table 2:- Age wise distribution of NLR in dengue patients.

AGE (years)	NLR<2	NLR>2	TOTAL	P value= 0.0005 (significant)
16-22	21	2	23	
23-28	18	10	28	
29-34	24	1	25	
35-40	6	2	8	
>40	7	9	16	
TOTAL	76	24	100	

Table-3 demonstrates that NLR<2 was noted in almost all the serological groups. This suggests that Dengue fever is associated with fall in NLR ratio. However, no statistical significance was noted.

Table 3:- NLR in relation with Dengue serology.

CASE STUDY	MALE	FEMALE	TOTAL	P value= 0.037 (significant)
NS1Ag	41	12	53	
NS1Ag, IgM	7	3	10	
NS1Ag, IgG, IgM	1	4	5	
IgG	15	3	18	
IgM	8	6	14	

In Table-4, it was observed that NLR was less than 2 when platelet count was below 60,000/µl. There was almost equal preponderance of NLR less than or higher than 2 in counts greater than 61,000/ µl. However, as platelet count improved the NLR rose suggesting normalising of differential counts. Therefore the count of 60,000 may be taken as a critical value for prognostication.

Table 4:- NLR in relation with platelet count.

PLATELET ($\times 10^3$ µL)	NLR<2	NLR>2	TOTAL	P value = 0.0369 (significant)
<20	2	0	2	
20-40	30	6	36	
40-60	16	3	19	
60-80	8	9	17	
>80	20	6	26	

In Table-5, it was noted that majority of male patients had low platelet counts. An overall male predominance (72%) of dengue infection was noted.

Table 5:- Gender wise distribution of platelets.

PLATELET ($\times 10^3$ µL)	MALE	FEMALE	TOTAL	P value = 0.799 (not significant)
<20	1	1	2	
20-40	28	8	36	
40-60	14	5	21	
60-80	11	6	17	
>80	18	8	26	
TOTAL	72	28	100	

Discussion:-

1. Dengue fever is an important arboviral disease of global concern causing major outbreaks with mortality and morbidity in endemic countries.[6]

2. In our study out of 100 patients, there was male preponderance. 72% cases were males and 28% cases were females. The male: female ratio is 2.5:1. This correlates with Vibha et al[7], Fu Xi Qui et al[8], Agarwal et al[9], Malathesha et al[10] and Banerjee et al[11] in which the male to female ratio is 2:1. This is due to the fact that males predominantly form the outdoor working population and more prone to infection by mosquito bite in a day time.

3. Majority of patients were in the age group of 23 to 28 yrs. This correlates with the study of Vibha et al.[7]

4. In the present study, majority of patients had thrombocytopenia with platelet count between the range of 20000-40000/µl. This correlates with the findings of Vibha et al.[7]

5. In a study by Padmanabhan P Athira et al, an arbitrary cut off of NLR was established as 2 and was found that on admission, a significantly higher proportion of dengue fever patients had NLR values < 2.0 (p=0.035) and monocyte lymphocyte ratio (MLR) ≥ 0.20 (p=0.0095) compared to children suffering from non-dengue febrile illness.[12]

6. In the present study, NLR was found to be less than 2 in 76% of dengue cases which was due to the presence of larger number of reactive lymphocytes.

7. Dengue patients had higher neutrophil percentage in first few days of fever, then this was reversed and percentage of lymphocytes increased. NLR in the dengue group was >1 on the first 5 days then reversed on day 6 to day 9.[13]

8. In the present study, NLR <2 was found in relation with very low platelet count of <40000 indicating severity of disease and NLR >2 was seen as the platelets improved and disease got better suggesting that NLR may be a prognostic indicator of dengue disease.

9. A higher NLR indicates a higher level of inflammation.[14] Therefore, NLR can be used to predict the severity of inflammation and also its prognosis.[15,16] Duffy BK et al, has reported higher rates of mortality among patients admitted to PICU with high NLR values.[15,16]

10. Yilmaz and Acar et al, 2017 had studied the diagnostic value of NLR in paediatric appendicitis among 658 patients and found the NLR to be raised in 17 patients with appendicitis with statistical significance.[17]

11. However, in the present study, contrasting findings of higher NLR in relation with higher platelet counts were observed. This was probably as the lymphocytosis and neutropenia seen in viral conditions was ameliorated with improvement of platelet counts.

Conclusion:-

1. The study concludes that NLR may be used as prognostic marker in management of dengue fever as lower NLR correlates with lower platelet counts and increasing NLR is observed with improving platelet counts suggesting the normalisation of differential count.

2. The platelet count of 60,000 with reference of NLR with cut off of 2 may be used to prognosticate the disease and take corrective therapeutic actions.

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