



## EFFECT ON TOTAL LEUCOCYTE COUNT AND SIGNIFICANCE OF TOTAL LEUCOCYTE AND PLATELETS WITH SEROSITIS IN ADULTS IN EARLY FEBRILE PERIOD OF NS1 ANTIGEN POSITIVE PATIENTS

### General Medicine

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### ABSTRACT

**OBJECTIVES:** To study the effect on total leucocyte count and their significance as well as of platelet count with serositis in patients of short duration febrile illness with NS1 antigen positivity.

**INTRODUCTION:** NS1 ANTIGEN was used to diagnose dengue infection and various flavivirus infections. Leucopenia, a well described feature is caused by bone marrow suppression by dengue virus. Selective leakage of plasma in pleural and peritoneal cavity due to functional change in vascular integrity.

**MATERIAL AND METHODS:** An observational study done retrospectively. Cases of febrile illness who tested positive for NS1 ANTIGEN (RDT) from the period of July 2018 to November 2018 were studied for presence of leucopenia, thrombocytopenia and serositis.

**RESULT:** leucopenia is a common finding in NS1 positive patients. However, there was no association seen of leucopenia or thrombocytopenia with presence of serositis

### KEYWORDS

NS1 Antigen, Leucopenia, Serositis, Thrombocytopenia

### INTRODUCTION

Ns1 Antigen (non structural protein - 1) test was introduced in 2006 and was used to diagnose Dengue infection as well as for differential diagnosis of various flavivirus infections (1). This test has a great deal of promise in the area of acute dengue diagnosis and is present in the serum of a person having recent dengue infection from day 1 of symptoms in contrast to IgM antibodies which appear some 5 or more days later. (2) The test NS1 Antigen can remain detectable up to 9 days following symptom onset. (3). The reported sensitivity of the non-structural protein 1 (NS1) antigen tests ranges between 48.5% and 58.6%, and the specificity ranges between 92.5% and 99.4%. The combined sensitivity of the dengue NS1 antigen and immunoglobulin M (IgM) antibody test increases to 89.9–92.9%, with a specificity of 75.0–88.8%. (4). Dengue virus detection can be done by a test which is nonstructural 1 (NS1) antigen, done in two ways: enzyme-linked immunosorbent assay (ELISA) and RDT formats. (5). Dengue virus belongs to the family Flaviviridae, characteristically called the breakbone fever and spreads by the bite of Aedes Mosquito. There are four distinct types which have been recognized (DEN1, DEN2, DEN3, DEN4). (6).

The clinical features of dengue vary with the age of the patient and, in addition to clinically inapparent infections, can be classified as non-specific febrile illness, classic Dengue, Dengue haemorrhagic fever, & dengue shock syndrome. (7).

However, WHO 2009 guidelines categorize dengue infection into dengue without warning signs (WS), dengue with WS, or severe dengue. The usual presentation of dengue fever is with nonspecific symptoms like fever, malaise, arthralgias, retroorbital pain, nausea and vomiting. Warning signs would include a) abdominal pain or tenderness, b) persistent vomiting, c) Evidence of serositis, d) mucosal bleeding, e) hematocrit rise ( $\geq 20\%$ ) with rapid drop in platelet count ( $< 50,000/\text{liter}$ ). Severe Dengue on the other hand includes warning signs with hypotension and one or more organ dysfunction. Dengue illness follows a natural course which is divided into three phases: a) Febrile phase which lasts 2-7 days, b) critical phase, c) Recovery phase. Patients who have no warning signs and are ambulatory should be

monitored for daily progression of symptoms, encouraged to take plenty of oral fluids and paracetamol. Patients with warning signs are admitted for in-hospital treatment, mainly staying in intravenous fluids and paracetamol. Antibiotics have no role until secondary bacterial infection is suspected. Severe dengue requires more aggressive management and admission in intensive care units as well as blood transfusion. (8)

It has been noted that leucopenia is a well described feature said to be caused by bone marrow suppression with dengue virus (9). Infact, new-onset leucopenia (WBC  $< 5,000$  cells/mm<sup>3</sup>) indicates that the symptoms may worsen within the next 24 hours and patient might go into the critical phase. (10) Thrombocytopenia in dengue infection may be associated with platelet dysfunction, increased destruction or consumption. In spite of haemorrhagic complications, thrombocytopenia may be associated with high chances of non-haemorrhagic complications like hepatitis, transaminitis, acute kidney injury, acute respiratory system syndrome etc. (11).

Data from various sources shows endothelial cell activation could mediate plasma leakage (12,13). Plasma leakage occurs due to functional rather than destructional effect on endothelial cell. The increased vascular permeability leads to contracted intravascular volume and shows in severe cases. Selected leakage of plasma in pleural and peritoneal cavity due to functional change in vascular integrity is mediated by various cytokines. (14)

### OBJECTIVE

To study the effect on total leucocyte count and their significance as well as of platelet count with serositis in patients of short duration febrile illness with NS1 antigen positivity.

### METHODOLOGY

The study was an observational study done retrospectively in SGT medical college, a multispecialty hospital in Budhera (gurugram), Harayana. Data was collected retrospectively in cases of acute febrile illness who tested positive for NS1 ANTIGEN (RDT) from the period of July 2018 to November 2018. Patients with acute febrile illness (1-5

days) with other associated symptoms such as malaise, headache, arthralgias, nausea, vomiting or abdominal pain were included in the study and subjected to tests for complete blood count, malaria antigen, peripheral smear for malaria, IgM typhidot, urine R/m, NS1 Antigen. Duration of fever > 5 days, positivity for malaria or typhidot or pus cells in urine, complicated febrile illness and any comorbidity such as hematological malignancy, steroid use, drugs causing leucopenia/leucocytosis, responsible for elevated or decreased leucocyte count was excluded from study. Out of all patients admitted with short duration fever 102 patients were positive for NS1 antigen. Daily total leucocyte count and platelet count was recorded. Vitals were monitored throughout the hospital stay and patients were conservatively managed with intravenous fluids and tab paracetamol. There was no hemodynamic instability or mortality observed.

### STATISTICAL ANALYSIS

Data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported for analysis on SPSS version 20.0. Results on continuous measurement are presented on Mean±SD (min-max) and results on categorical measurements are presented in number (%). Chi square test was used to determine association between categorical variables. P value less than 0.05 was considered significant.

### RESULT

The study was an observational study. NS1 Antigen positive patients in those presenting with short duration febrile illness (1-5) days > 18 years of age were included in the study. Total number of patients after applying the exclusion criteria were 97 in number out of 102 positive cases of NS1 ANTIGEN. 9 went LAMA while 7 absconded. Hence, the number of patients finally included in the study were 81. Out of 81 patients 37 were female and 44 male, distribution of which has been shown in Table 1

**TABLE 1**

Gender	no of patients	%
Female	37	45.67
Male	44	54.32

### BLOOD COUNTS OF PATIENTS STUDIED

TOTAL LEUCOCYTE COUNT (per cubic mililitre)	NUMBER OF PATIENTS (n=81)	%	MEAN ± SD
<4000	45	55.56	2891.11±584.97
4000-11000	32	39.5	5287.5±1572.50
>11000	04	4.93	12825±899.54

### PROFILE OF TOTAL LEUCOCYTE COUNT WITH SEROSITIS

LEUCOCYTE COUNT (per cubic mililitre)	PRESENCE OF SEROSITIS	%	P VALUE
< 4000 (45)	6	13.33%	0.518 (NS)
4000 -11000 (32)	6	18.75%	
>11000 (4)	NIL	nil	NA

Serositis in comparison with leucopenia and normal leucocyte count statistically found to be not significant (P>0.05).

### PROFILE OF PLATELET COUNT WITH SEROSITIS

PLATELET COUNT (per cubic mililitre)	PRESENCE OF SEROSITIS	%	P VALUE
< 1.5 lakh (51)	8	15.4%	0.773 (NS)
1.5-4 lakhs (30)	4	13.33%	

Serositis on comparison with thrombocytopenia and normal platelet count was statistically found to be not significant (P>0.05).

### DISCUSSION

In our study, there were 37 female (45.67%) and 44 males (62%). The male to female ratio was 1.9:1. In a study by Nagaram PP et al about 174 confirmed cases of dengue were included with 95 (95.67%) males and 79 (45.47%) females and the male to female ratio was 1.2:1 (15).

In our study 45 patients out of 81 had leucopenia (<4000) which is 55.56% of total patients. 32 had normal leucocytes which is 39.5% of total patients, and 4 had leucocytosis (>11000) making 4.937% of total patients. In a study by Nagaram PP et al (15) out of 174 cases, 96 had leucopenia (55.17%), 26 cases had leucocytosis (14.94%) while 52 cases had normal leucocyte count (29.89%). In another study by

Christopher et al (16) out of 284 patients enrolled in the study 87% dengue patients had leucopenia which was much more significant than any other infection. In another study, out of 99 patients with dengue fever, 44 patients had leucopenia (17).

In our study, serositis was present in 12 out of 81 patients making 14.8%. Ejaz et al in their study reported pleural effusion in ten out of 79 patients (12.6%) (18).

In our study, when we correlated the leucocyte count with serositis, we found that only 6 had serositis out of 45 patients of leucopenia (13.33%) and out of 32 patients of normal leucocyte count again 6 had serositis (18.75%). It was statistically also found that there is no correlation of serositis with leucocyte count.

In our study when we correlated the platelet count with serositis we found that in 51 patients of thrombocytopenia only 8 had serositis (15.4%) and in 30 patients of normal platelet count only 4 had serositis (13.33%). Statistically there is no correlation noted of serositis with platelet count.

### CONCLUSION

According to our study, NS1 positive patients in early febrile period show majority having leucopenia followed by normal leucocyte count. When leucocyte count is correlated with serositis we found no correlation and statistically also it's not significant. Similarly, when we correlated platelets with serositis, although there is a slight higher number of cases of serositis in patients having thrombocytopenia than those with normal platelet count but again this is not statistically significant.

### REFERENCES

- CDC-Laboratory Guidance-Dengue ([http://www.cdc.gov/dengue/clinical\\_lab\\_laboratory.html](http://www.cdc.gov/dengue/clinical_lab_laboratory.html)). www.cdc.gov. Retrieved 2015-12-01
- Bio Rad Launches Test for Early Diagnosis of the Dengue Virus (<http://www.selectscience.net/product-news/bio-rad-laboratories-informatics-division/bio-rad-launches-test-for-early-diagnosis-of-the-dengue-virus?artID=9997>)
- Kin Fai Tang & Eng Eong Ooi (2012) Diagnosis of dengue: an update, Expert Review of Anti-infective Therapy, 10:8, 895-907, DOI: 10.1586/eri.12.76
- Blacksell SD, Jarman RG, Bailey MS, Tanganuchitcharnchai A, Jenjaroen K, Gibbons RV, Paris DH, Premaratna R, de Silva HJ, Laloo DG, Day NP. Evaluation of six commercial point-of-care tests for diagnosis of acute dengue infections: the need for combining NS1 antigen and IgM/IgG antibody detection to achieve acceptable levels of accuracy. Clin Vaccine Immunol. 2011;18:2095-2101.
- Dussart P, et al. 2008. Evaluation of two new commercial tests for the diagnosis of acute dengue virus infection using NS1 antigen detection in human serum. PLoS Negl. Trop. Dis. 2:e280.
- Jayanta Samanta and Vishal Sharma. Dengue and its effects on liver. World J Clin Cases. 2015 Feb 16; 3(2): 125-131.
- Gibbons RV and Vaughn D.W. Dengue: an escalating problem. BMJ. 2002 Jun 29; 324(7353): 1563-1566.
- World Health Organization. Dengue: Guidelines for diagnosis, treatment, prevention and control. Geneva: 2009.
- LaRussa VF, Innis BL. Mechanisms of dengue virus-induced bone marrow suppression. Baillieres Clin Haematol 1995;8:249-70.
- CDC. Clinical guidelines for the management of dengue infection. Revised November 2015. US Department of health and human services. GA. USA. Available from [https://www.cdc.gov/dengue/clinical\\_lab/clinical.html](https://www.cdc.gov/dengue/clinical_lab/clinical.html). Accessed October 12, 2017.
- Hari Kishan Jayanthi, Sai Krishna Tul. Correlation study between platelet count, leukocyte count, nonhemorrhagic complications, and duration of hospital stay in dengue fever with thrombocytopenia. J Family Med Prim Care. 2016 Jan-Mar; 5(1): 120-123.
- Avirutnan P, Malasit P, Seliger B, Bhakdi S, Husmann M. Dengue virus infection of human endothelial cells leads to chemokine production, complement activation, and apoptosis. J Immunol. 1998;161:6338-46.
- Cardier JE, Mariño E, Romano E, Taylor P, Liprandi F, Bosch N, et al. Proinflammatory factors present in sera from patients with acute dengue infection induce activation and apoptosis of human microvascular endothelial cells: Possible role of TNF-alpha in endothelial cell damage in dengue. Cytokine. 2005;30:359-65.
- DB Kadam, Sonali Salvi, Ajay Chandanwale. Expanded Dengue. Journal of The Association of Physicians of India. July 2016; vol 64; 59-63.
- Nagaram PP, Pidugu P, Munagala VK, Matli VV. Clinical and laboratory profile and outcome of dengue cases among children attending a tertiary care hospital of South India. Int J Contemp Pediatr. 2017; 4: 1074-80. doi: 10.18203/2349-3291.ijcp20171731.
- Gregory CJ, Lorenzi OD, Colón L, García AS, Santiago LM, Rivera RC, Bermúdez LJ, Báez FO, Aponte DV, Tomashuk KM, Gutierrez J, Alvarado L. Utility of the tourniquet test and the white blood cell count to differentiate dengue among acute febrile illnesses in the emergency room. PLo S Negl Trop Dis. 2011 Dec; 5(12): e1400. doi: 10.1371/journal.pntd.0001400. Epub 2011 Dec 6.
- Jayanthi HK, Tulasi SK. Correlation study between platelet count, leukocyte count, nonhemorrhagic complications, and duration of hospital stay in dengue fever with thrombocytopenia. Journal of Family Medicine and Primary Care. 2016; 5(1): 120-123.
- Ejaz K, Khursheed M, Raza A. Pleural effusion in dengue. Karadu perspective Saud Med Journal. 2011; 32(1): 46-9.