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General Medicine

THE DYNAMICS OF HAEMATOLOGY AND BIOCHEMISTRY PROFILE IN DENGUE INFECTION

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ABSTRACT Dengue fever is most common tropical disease, which spreads by arthropod borne vectors, becoming global burden in southeast asia. This study aims to know the haemotological and laboratory findings ,which helps in guiding the timely intervention in future.

KEYWORDS : Thrombocytopenia, Dengue Haemorrhagic fever, Dengue Shock Syndrome, NS1Ag-Non Structural Antigen.

1.INTRODUCTION:

Dengue is a mosquito borne viral disease, which has raised concern globally due to alarming 3 fold increase in its incidents in the last few decades and in the present decade , spreading from urban to rural settings. It is caused by dengue virus (DENV), RNA containing enveloped virus –which belongs to family Flaviviridae and its transmission by the Aedes mosquito, especially Aedes aegypti.

Dengue is a self limiting acute disease of fever, muscle joint pains, rash, nausea and vomiting. Infection with any one of four serotypes might cause a spectrum of clinically symptomatic disease ranging from an undifferentiated fever to acute febrile illness-such as dengue haemorrhagic fever (DHF) or dengue shock syndrome(DSS).

The period of transmission from humans to mosquitoes begins one day before the start of fever up to the sixth day of illness corresponding to the viremia phase. After a female bites an individual in the viremia phase, viral replication (extrinsic incubation) begins in the vector from eight to twelve days. In humans, the incubation period ranges from 3 to 15 days (intrinsic incubation) with an average of 5 days.

The diagnosis of dengue fever is carried out based on clinical, epidemiological and laboratory data. Among laboratory tests, both non-specific [blood count, platelet count, tourniquet test, prothrombin time (PT), activated partial thromboplastin time (APTT), liver function tests and serum albumin concentration] and specific tests (viral isolation tests and serology for antibody examination) are used.

Leukopenia is the most prominent hematological change, sometimes with counts of less than 2 x 10^3/µL. However, there are reports of mild leukocytosis at the onset of the disease, with neutrophilia. Lymphocytosis is a common finding, with the presence of atypical lymphocytes. The haematocrit concentration should be monitored according to the days of illness, remembering that, with the progression to DHF, there will be a 20% increase in hematocrit from the patient's baseline, associated with thrombocytopenia (< 100 x 10^9/L).

Of biochemical variables, the most frequent changes occur in liver function tests such as in serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), Gamma-glutamyl transpeptidase and alkaline phosphatase levels, and serum albumin.

2. AIMS AND OBJECTIVES OF STUDY: The present study aimed to assess the biochemical and hematological dynamics of patients with dengue fever in the most serious cases and to identify laboratory markers that may indicate this evolution.

3. MATERIALS AND METHODS:

Study Area: The study is conducted in the department of General Medicine ASRAM Hospital, Eluru.

Period Of Study: The study was conducted between September 2016 to December 2018. Patients were classified into classic dengue fever (CD), dengue hemorrhagic fever (DHF) and dengue shock syndrome according to WHO criteria (2009). The first day of the disease was considered the onset of symptoms related to dengue fever and the laboratory profile was evaluated for the first 12 days.

Design Of Study: Prospective study.

Sample Size: The study population was 132 patients, admitted to this hospital with clinical and laboratory evidence. The variables selected for the study were: Hemoglobin (Hb), Haematocrit (Ht), Leukocytes and Lymphocytes count, Platelets count, ALT and AST enzymes.

Selection Criteria: Patients with clinical picture of dengue fever with serologically confirmed by NS1Ag/IgM/IgG were included and Patients with other co-infections like Leptospirosis, Malaria etc.,Chronic Renal and liver failure patients were excluded Informed consent was obtained from the patients. And the data was analysed using SPSS software.

RESULTS:

The results of 132 patients with clinical and laboratory diagnosis of dengue fever were analyzed; 43 (32.57%) were female and 89 (67.42%) were male. The ages ranged from 16 to 85 years. Regarding the clinical form of the disease, of 89 male patients 64 cases were dengue fever, 21 cases were Dengue haemorrhagic fever, and 3 cases were of Dengue shock syndrome.

Of the female patients, 31 cases were of dengue fever and 13 cases are of DHS.95 cases are dengue fever,34 cases are DHS and 3 cases are of DSS.

Complete Hemogram, Liver function tests, Renal function tests were done. These investigations were analyzed as in **Table 1.**

Mean Hematocrit was 40% and haematocrit was classified into low or high based on the reference standards – males : 38.8 – 46.4%, females : 35.4 – 44.4 %.Among the laboratory features, haematocrit was found to be statistically significant in DHF patients. 61 patients were found to have haematocrit of >40% and 71 patients were found to have ≤40%. Raised Serum aminotransferase level (> 2 times upper normal value) was seen in 23 cases (17.4%) of which 17 cases (17.8%) were of DF and six cases (16.2%) were of DHF. Mean levels of AST & ALT calculated was 80 & 75 respectively. Leukopenia was found in 40(30.3%) cases in which 28 cases are of DF and 12 cases are of DHF.

Lab parameters	Total(n=132) % (n)	DF(n=95) % (n)	DHF(n=37) %(n)	P value
TLC ≤4000	30.3(40)	29.4(28)	32.4(12)	0.52
PCV ≥40	46(61)	43(41)	54(20)	0.02
PLATELET COUNT≤1 LAKH	47(63)	41(39)	64.8(24)	0.03
AST ≥ 2 UNL	17.4(23)	17.8(17)	16.2(6)	0.57
ALT≥2 UNL	17.4(23)	17.8(17)	16.2(6)	0.98

63 patients (47%) had platelet count <1,00,000. Among these, 39 cases (41%) were of DF and 24 cases (64.8%) were of DHF as in **Table 2** Mean platelet count calculated was 1.21 lakhs/mm3.

Thrombocytopenia was significant finding in patients of severe dengue as compared to DF (p-value<0.05**) (Table 2).**Thrombocytopenia was seen in 39cases (41%) of DF, 24cases (64.8%) of DHF & DSS. Patients having platelet count of < 20000 were 9 (6.8%), 20000-50000 were 13 (9.8 %), 50000-100000 were 41(31%) and > 1 lakh were 69(52.2%).

The level of thrombocytopenia was in concordance with the severity of dengue infection but there was poor relation between the level of thrombocytopenia and bleeding tendency as patients of DF who did not bleed had thrombocytopenia and in patients of DHF, bleeding manifestations did not occur even if the platelet count was less than 20000/mm3.

Platelet count	Total (132) %(n)	Dengue fever (n=95)	DHF&DSS(n=37)
Less than 1 lakh	47(63)	41(39)	64.8(29)
More than 1 lakh	53(70)	60(57)	35.1(13)

DENGUE NS1 AND SEROLOGY TESTING :
NS 1 Ag only was positive in 57cases (43.1%), IgM Ab only was positive in 8 cases (6%), both NS1 &IgM was positive in 36cases (27.2%), both NS 1 and IgG was positive in 6

cases (4.5%), both IgM & IgG were positive in three cases (2.2%), NS1Ag, IgM & IgG all three were positive in 22 cases (16%).

Mortality was not seen in cases of Classical dengue fever, DHF and DSS.

5. DISCUSSION:
Due to the lack of studies of varied clinical manifestations and lab results of diseases in India and across the world, especially tropical diseases like dengue, there has been a paucity of adequate studies to compare our results with.

In present study, thrombocytopenia(platelet count < 1 lakh/mm3as per WHO criteria) was present in 62(47%) cases. In studies done by Singh NP et al, Anuradha M et al103 and Nandini Chatterjee et al96 thrombocytopenia was observed in 62%, 60% and 55.5% respectively. The levels of AST and ALT (>2 times upper normal value) were elevated in 23(17.4%) cases, analogous findings were observed by Singh NP et al94(16%). However, in a

study done by Anuradha M et al103, AST was raised in 43% and ALT was raised in 40% cases and in a study done by Nandini Chatterjee et al96, ALT level was raised in 77.2% patients. The levels of AST were equal to or greater than those of ALT levels in all of dengue

infected patients, findings at par with Ritu Karoli et al91and Khan AH et al100 in their study. However the findings in our study were 16% as compared to 86%. As per WHO 2009 guidelines, elevation of AST and ALT >1000 U/L was criteria for severe dengue. In our study, in none of the patients AST/ALT were >1000 U/L. Although aminotransferase levels increase in conjunction with dengue severity, AST/ALT levels did not discriminate DF and DHF as per study of Lee et al, reflecting a similar result in our study. Leukopenia(WBC<4000/mm3) was found in 40(30.3%) cases, similar to that observed by Nandini Chatterjee et al96, AnuradhaM et al103(40%) and Rachel Daniel et al93(32.7%) but lower than that observed by Singh NP et al94(68%).

6.CONCLUSION:
Among the laboratory features, thrombocytopenia and hematocrit were found to be statistically significant in DHF patients. 61 patients were found to have hematocrit of >40% and 71 patients were found to have ≤40%. Mean Hematocrit was 40%. 63 (47%) patients had platelet count <1,00,000. Among these, 39 cases (41%) belong to DF and 24 cases (64.8%) belong to DHF. Mean platelet count calculated was 1.21 lakhs. The level of thrombocytopenia was in concordance with the severity of dengue infection, but there was poor relation between the level of thrombocytopenia and bleeding tendency.

Leukopenia was found in 40(30.3%) cases in which 28 cases are of DF and 12 cases are of DHF. Raised Serum Aminotransferase level (> 2 times upper normal value) was seen in 23 cases (17.4%) of which 17 cases (17.8%) were of DF and six cases (16.2%) were of DHF.

It is important to recognize the signs and symptoms at the earliest, alteration in biochemical parameters and multisystem involvement pattern in dengue to reduce the mortality. A focused history, detailed clinical examination and appropriate relevant investigations can aid for early diagnosis and treatment. Apart from typical manifestations, atypical presentations are on rise, which makes the diagnosis even more challenging and interesting for researchers. Continuous surveillance and timely interventions will minimize the complications, outbreak and mortality.

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