PATHOPHYSIOLOGICAL BASIS OF HAEMATOLOGICAL PROFILE OF DENGUE FEVER.

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Abstract: **Background:** Dengue is a self-limiting acute viral disease characterized by fever, muscle & joint pains, headache, rash, nausea & vomiting. It is transmitted by female mosquitoes mainly of the species Aedes aegypti and less by, Aedes albopictus. Dengue virus infection may be asymptomatic or may cause undifferentiated febrile illness (viral syndrome), dengue fever (DF), or dengue haemorrhagic fever (DHF) including dengue shock syndrome (DSS). **Objectives:** To evaluate the haematological profile for early clinical diagnosis & prompt management. **Methods:** Study was done in 100 patients diagnosed as dengue fever. IgM positive or NS 1 positive patients of dengue fever with age group between 18-60 years patients were taken. Parameters of haematological profile was taken in all patients. **Result:** Out of 100 patients, 22% had mild thrombocytopenia, 47% had moderate thrombocytopenia and 29% had severe thrombocytopenia. Overall 98% of patients had thrombocytopenia. About haematocrit, 36% patients having haematocrit below 40% and 49 % of patients having haematocrit between 40 to 45%, and only 15 % of patients having haematocrit above 45%. Leucopenia was seen in 29 % of patients. **Conclusion:** Thrombocytopenia was key finding in our study & other associated findings included leucopenia, rise in haematocrit.

Key Words: Dengue fever,Thrombocytopenia,Haematocrit,Haematological profile.

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Introduction:

Dengue is one disease entity with different clinical presentations, often with unpredictable clinical evolution and outcome"[1].Dengue is a self-limiting acute viral disease characterized by fever, muscle & joint pains, headache, rash, nausea & vomiting [2]. It is transmitted by female mosquitoes mainly of the species Aedes aegypti and less by, Aedes albopictus.[3] Dengue virus infection may be asymptomatic or may cause undifferentiated febrile illness (viral syndrome), dengue fever (DF), or dengue haemorrhagic fever (DHF) including dengue shock syndrome (DSS).[4]

The origins of the word dengue are not clear, but one theory is that it is derived from the Swahili phrase "Ka-dinga pepo", meaning "cramp-like seizure caused by an evil spirit". The Swahili word "dinga" may possibly have its origin in the Spanish word "dengue" meaning fastidious or careful, which would describe the gait of a person suffering the bone pain of dengue fever. Slaves in the West Indies who contracted dengue were said to have the posture and gait of a dandy, and the disease was known as "Dandy Fever".[5]

The first confirmed case report dates from 1789 and is by Benjamin Rush, who coined the term "Breakbone fever" because of the symptoms of myalgia and arthralgia.[5,6] The first confirmed epidemic of DHF was recorded in the Philippines in 1953–1954 and in Thailand in 1958.The first evidence of occurrence of DF in India was reported during 1956 from Vellore district in Tamil Nadu. The first DHF outbreak occurred in Calcutta (West Bengal) in 1963 with 30% of cases showing haemorrhagic manifestations.[6]

The Incidence of dengue has grown dramatically around the world in recent decades[3].In india, the risk of dengue has increased in recent years due to rapid urbanization, and deficient water management including improper water storage practices in urban, peri-urban and rural areas, leading to proliferation of mosquito breeding Sites[7].

Based on the dengue transmission potential at macro and micro levels,WHO has categorized the Countries in SEARO. Till 2009, India was in Category B. However, in view of increasing endemicity, WHO, in 2010, grouped India in Category A, where Dengue is a major public health problem, hyperendemicity in urban centres spreading to rural areas and multiple virus serotypes circulating.[2] However, in Gujarat the transmission is perennial.[7]

Presently, there is no specific anti viral drug or vaccine against dengue infection.[2,7] For, early recognition of dengue cases, pathophysiology of haematological profile is useful and support early clinical diagnosis & prompt management.

Material and Methods:

Study was done in P.D.U govt. Medical college & hospital, Rajkot, after taking permission from Institutional Ethics Committee. In this study, we took 100 patients admitted in the hospital and diagnosed as having dengue fever. Patient's consent was taken. In our study, IgM positive or NS 1 positive patients of dengue fever with age group between 18-60 years patients was taken. Patients with pregnancy, pre-existing chronic liver,kidney or heart disease & h/o of hematological disorders were excluded. In our study, detailed histoy, clinical examination & haematological profile taken. Parameters of haematological profile were measured in automated haematology analyzer in pathology department.

Result:

Following haematological profile parameters were get from our study .

Table-1: Age & Sex distribution in dengue fever.

Age (years)	No.of cases			% of cases
	M	F	Total	
18-30	53	18	71	71%
31-40	9	6	15	15%
41-50	4	4	8	8%
51-60	5	1	6	6%
Total	71	29	100	100%

In our study, most of the cases belong to the age group 18-30 years. 71 cases are from 18-30 years age group, as dengue is seen more in younger age group. 15 are between 31-40 years age group, 8 are from 41- 50 years age group and 6 are between 51-60 years age group.

Table-2: Platelet count in dengue fever.

Platelet Count (Lacs/mm^3)	No.of cases	% of cases
>1.5	2	2%
1.5-1.0	22	22%
1.0-0.5	47	47%
<0.5	29	29%
Total	100	100%

This study shows 22% had mild thrombocytopenia, 47% had moderate thrombocytopenia and 29% had severe thrombocytopenia. Overall 98% of patients had thrombocytopenia.

Table-3: Haematocrit in dengue fever .

Haematocrit (%)	No.of cases	% of cases
Below 40	36	36%
40-45	49	49%
Above 45	15	15%
Total	100	100%

In our study, 36% patients having haematocrit below 40%and 49 % of patients having haematocrit between 40 to 45%, and only 15 % of patients having haematocrit above 45%.

Table-4: Total leucocyte count in dengue fever.

Total leucocyte count(Cells/mm^3)	No.of cases	% of cases
Below 4000	29	29 %
4000-11000	68	68%
Above 11000	3	3%
Total	100	100%

In present study, 68% patients had Total count between 4000-11000 cells/cumm.

Leucopenia was seen in 29 % of patients and only 3% was seen leucocytosis.

Discussion:

A total of 100 patients admitted to our hospital with IgM or NS1 dengue positive cases studied. Out of which 71 male patients and 29 female patients are affected. The male to female ratio is 2.44:1. Our study is consistent with other studies, study done by Butt N et al[8], male to female ratio is 3:1. And also study done by Neerja M et al[9], the male to female ratio is 2:1.

In present study, Maximum no. of patients (71%) affected between 18-30 years age group. In study done by Ghosh G et al[10], mean age group affected was 21-30 years. In Farhan F & Birdar S[11] study, maximum cases were affected from the age group 21-30 years. Dengue is seen more in younger age group.

Our study shows 22% had mild thrombocytopenia, 47% had moderate thrombocytopenia and 29% had severe thrombocytopenia. Overall 98% of patients had thrombocytopenia. In Syed Anjum Mehndi et al[12] study, there were 100% - all patients had thrombocytopenia. In study done by Butt N et al[8], also there were thrombocytopenia in 100% cases.

The pathophysiology of dengue infections are abnormal haemostasis and plasma leakage.[13] The abnormalities in haemostasis seen in dengue infections involve all its major components including: (1) vasculopathy; (2) thrombopathy, with impaired platelet function and moderate to severe thrombocytopenia; (3)coagulopathy, with activation of the coagulation system and fibrinolysis, plus in the later stages of severe disease; disseminated intravascular coagulation (DIC); (4) bone marrow changes, including depression of all marrow elements, with maturation arrest of megakaryocytes during the early phase of the illness, which is reversed after defervescence. The most consistent finding in dengue infections is a transient thrombocytopenia. The exact underlying mechanism remains unclear. Studies suggest it is multifactorial, including: suppression of megakaryocytopoiesis, and increased platelet clearance by DENV-induced apoptosis and antiplatelet antibodies.[13]

In present study, 76% had moderate to severe (< 1lacs/cumm) thrombocytopenia and 22% had mild thrombocytopenia. In study done by Malathesa M & Ashwini H[14], 80.49% had moderate to severe (<1lacs/cumm) thrombocytopenia and 19.4% had mild thrombocytopenia. In study of Pavan kumar M et al.[15], there were 90% of patients having mod to severe thrombocytopenia of less than 1lacs /cumm. Above all study finding supports our present study. The most common abnormality seen in our patients was thrombocytopenia, as observed in above other studies.[8,10,11,12,14,15] Thrombocytopenia is a key clinical finding in dengue patients during the course of viremia.

This is thought to be due to depression of bone marrow observed in acute stage of dengue virus infection.[14] Other explanations are direct infection of the megakaryocytes by virus leading to increased destruction of the platelets or the presence of antibodies directed against the platelets. Thrombocytopenia may result from destruction of peripheral platelet or bone marrow megakaryocytes by viruses which consequently reduce the platelet production.[14,16]

In our study, 36% patients had haematocrit below 40% and 49 % of patients having haematocrit between 40 to 45%, and 15 % of patients had haematocrit above 45%. Our study is in tune with Farhan F & Birdar S[11]study, 19% of patients had greater than 45% hct and 54 % patients had hct between 40-45%. It also in tune with study done by Rachel Daniel et al[17], there were 27.9% patients having hct greater than 45%.

Clinical evidence supporting plasma leakage includes a rapid rise in haematocrit, hypo-proteinaemia, pleural effusions and ascites and reduced plasma volume, leading to haemodynamic compromise and hypovolaemic shock[13].In our study, it was found that the haematocrit rise was seen in many cases. But also various pitfalls of Hct are non availability of pre-illness hematocrit, High prevalence of anemia in the Indian population, blunting of hemoconcentration due to early institution of fluid therapy and a fall in haematocrit if there has been significant blood loss[18].

In present study, 68% patients had total count between 4000-11000 cells/cumm. Leucopenia was observed in 29 % of patients and only 3% had leucocytosis. Our study is corresponds with the study done by Malathesa M & Ashwini H[14],showing leucopenia in 27.6% patients and in a study done by Kirtilaxmi K et al[19], 37% of patients had leucopenia. In studies done by Neerja M et al [9], 22% of patients had leucopenia. Leucopenia in dengue fever is due to direct bone marrow suppression by the virus.[4,13,18,19.]

Conclusion:

The following conclusions were derived from our data of present study:
Dengue fever affects males about 2.44 times more than females. It affects more in younger age group. Basic hematological parameters can be used as indicators of dengue infections, in which, Thrombocytopenia was key finding in our and other previous studies also. Other associated findings included leucopenia, rise in haematocrit.

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