A study of Clinico-Haematological and Therapeutic Profile of Dengue Fever

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Abstract :

Introduction : Dengue fever caused by Flavivirus is a common ailment inflicting the population. The easy transmission by means of mosquito bites makes it all the more threatening. Objectives: To study and establish clinical and haematological correlation with management profile of dengue viral infection. **Materials & Methods:** A study of 71 indoor sero-positive dengue fever cases was done retrospectively. Clinical features and haematology reports were collected and analyzed statistically. Hospitalization duration and therapeutic management data were collected and analyzed. **Results:** Total 308 clinically suspected patients' blood samples were tested at a tertiary care level hospital; out of which 71 (23.5%) patients were positive for acute dengue fever. Female: male ratio, and adult:old ratio was 1.15:1 and 4.6:1, respectively. A maximum 70.4% case of dengue fever were recorded between September and December 2014. Clinically, fever was the commonest symptom presentation in 97.2% patients, followed by muscle pain and vomiting in 87.3% and 78.8%, respectively. Least common clinical presentation was skin rashes and haemorrhagic manifestations in 1.4% cases each. Anaemia, leucopoenia and thrombocytopenia were noted in 57(80%), 33 (46%) and 52 (73.2%) of patients, respectively. The associated diseases were noted in 28 (39%) patients and responsible for 3 (4.2%) deaths. Antipyretics, antiemetics, proton pump inhibitors and IV fluids were main therapy. Hospitalisation day average was 6.1 days/patient. **Conclusion:** High grade fever, muscle pain, vomiting, anemia, leucopoenia with lymphocytosis, thrombocytopenia were detected commonly, while rashes, shock and haemorrhagic diathesis were rare complications in primary dengue fever cases. The associated clinical conditions i.e., malaria, enteric fever etc. should be looked, they might be responsible for complications in primary dengue fever cases.

Key words : Clinico-haematological, Dengue, Therapy

Introduction :

Dengue fever (DF) is a febrile illness caused by a RNA flavivirus. Viruses are transmitted by female Aedes egypti or rarely by Aedes albopictus mosquito. The mosquitoes breed in stored clean water near human residence and inside room i.e. flower pot, water coolers, air conditioners etc., and it bites during day times. Aedes egypti primarily lives in the tropical and sub tropical region.[1] The viruses are found within salivary glands of the mosquitoes which allows it to survive from season to season. There are 4 serotypes (subtypes) namely DENV1, DENV2, DENV3 and DENV4. In Southeast Asia, dengue fever is due to two DENV2 subtype viruses. Each virus serotype provides specific lifetime immunity by homotypic neutralising antibody and short term cross immunity by heterotypic non neutralising antibody. [2] The acquired immune response to dengue infection varies and depends on primary or secondary infection. Primary immune response was seen in individuals who were not immune to dengue and secondary immune response was observed in patients who have had a previous dengue infection. Dengue fever begins after average 4-7 days of incubation. [1] The symptoms of classic dengue fever are fever, muscle pain, retro bulbar pain, severe joint pain, swollen lymphnodes and rashes. Dengue Haemorragic Fever (DHF) is a more severe form of viral fever and common in children. DHF is commonly due to secondary infection of DENV2 virus preceded by DENV1 virus infection. Secondary DF occurs at 5 to 20 years interval after primary infection. Pre-existing antibody from DENV1 virus infection fails to neutralise DENV2 virus and may enhance viral uptake and replication in mononuclear phagocytes.[3] These phenomena may result in activation of mediators and complements and clotting cascades leading to DHF. Its symptoms are severe headache, fever, rashes and evidences of haemorrhage in the body e.g. petechiae (small red or purple spots or blisters under the skin, bleeding nose or gums, black stools, easy bruising). On

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application of tourniquet on limb, petechiae appear on distal part of the limb. Dengue Shock Syndrome (DSS) may be due to sudden increase in permeability of capillaries. It is associated with oedema and serositis e.g. pleural effusion and or ascites. DSS may last for 48 hours and it is a grave complication if not treated in time.[4] Dengue fever is diagnosed by IgM antibody detection by ELISA or paired serology or detection of antigen by ELISA or RT- PCR during acute phase. IgG antibody positive suggests past infection. Management of dengue fever is symptomatic with antipyretics i.e. paracetamol without non steroidal anti inflammatory drugs (NSAID), fluid therapy, platelet replacement not needed. DHF should be treated with blood transfusion and DSS by optimising fluid therapy rapidly. [5]

Materials & Methods :

Total 308 patients' blood samples were collected from OPD or IPD between 1stJanuary 2014 to 31st December 2014 at a tertiary care level hospital and all blood samples were tested for dengue fever profile. Blood samples were collected with standard laboratory precautions. All samples were tested for Qualitative capture ELISA IgM antibody, Qualitative capture ELISA IgG antibody and NS1 antigen detection by Rapid serological test (Card method). The patients having IgM antibody and/or NS1 antigen in blood were isolated and listed as dengue fever cases. [6] All the indoor cases of DF patients were analyzed in a structured performa. The performa included the information of patient's registration data, clinical features, investigation profile i.e. laboratory investigations and imaging investigations in detail. The therapeutic management data including fluid therapy, antipyretic, antibiotic, antimalarial therapy or other therapies were noted and analyzed statistically. The duration of hospitalisation and associated diseases were also recorded and analyzed with other data. Indoor patients with NS1 antigen and/or IgM antibody positive were included in study as acute dengue viral infection cases. Patients with only IgG antibody in blood were excluded as it suggests old dengue viral infection.

Results :

The clinically suspected 308 cases of DF were tested for dengue profile; 71 cases (23.1%) were positive, i.e., either NS1 antigen and/or anti IgM antibody positive, for acute dengue fever. [7] Age distribution shows, the patients below 40 years and above 40 years were 58 (81.7%), and 13 (18.3%), respectively.

Table 1: Comparison of study at different tertiary care hospitals

Variables	Present study GCS Hospital	Study at L.G. Hospital [6]	Study at Pune [10]
Study Duration	Jan14 to Dec14	Oct13 to Jan13	Nov.12 to April12
No. of the samples Tested/Positive for dengue fever cases (%)	308/71 (23.5%)	169/44 (26%)	452/98 (21.6%)
Most common symptoms cases (%)			
Fever	69 (97.20%)	56 (88.60%)	67 (95%)
Bodyache	62 (87.30%)	53 (75%)	62 (87.3%)
Vomiting	56 (78.80%)	69%	54 (76%)
Platelet count			
F<50000/L	22 (30.90%)	26 (36.30%)	41 (57%)
50000-150000/	30 (42.30)%	32 (44.90%)	17 (24.10%)
L>150000/L	14 (19%)	13 (18.80%)	13 (18.90%)

As shown in Table 1, the clinically suspected cases presented with high grade fever with severe bodyache and thrombocytopenia.

Table 2: Laboratory data of Dengue fever cases

Haemoglobin & Anaemia	Hb Level(g/dL)	Cases (%)
Normal	>12	14(20%)
Mild	9-12	37(57.2%)
Moderate	7-9	10(14.1%)
Severe	<7	10(14.1%)
Leucocytes	Total count(/cmm)	Cases (%)
Leucopenia	<4000	33(46.5%)
Normal leucocytes	4000-11000	31(43.5%)
Leukocytosis	>11000	7((10%)

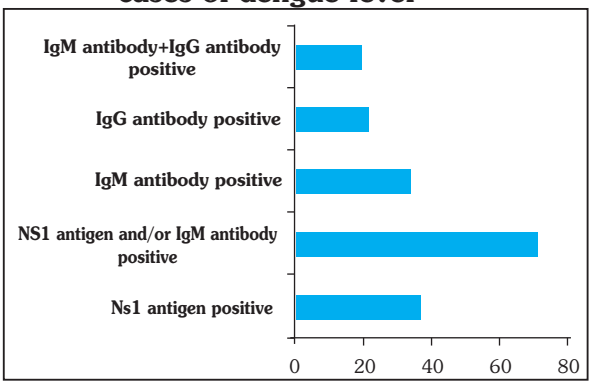
As shown in Table 2, anaemia & leucopoenia were noted in 57 cases (80.28%) and 33 cases (46.5%), respectively.

Table 3: Duration of Hospitalisation

Hospitalisation duration	Cases(%)
Days 1—3	24(33.8%)
Days 3—7	36(50.7%)
Days >7 with associated disease	10(14.1%)
Days >7 without associated disease	1(1.4%)

Table 3 shows, 60 cases (84.5%) were indoor for a range of 1-7 days; suggesting a brief period of hospitalisation for symptomatic treatment, while more than 7 days hospitalisation was noted in 10 cases (14.1%) with associated disease, and in 1 case (1.4%) without associated disease. Antipyretic therapy and antiemetic drugs with proton pump inhibitors or H_2 blockers were administered in 68(95%) cases, 48(67.7%) cases and 64(90.9%) cases, respectively.

Figure 1: Immunological data* of 71 positive cases of dengue fever



*- Multiple responses

Figure 1 shows that 71 cases (23.1%) were positive as per the diagnostic criteria; i.e., either NS1 antigen and/or anti IgM antibody positive for acute dengue fever.

Discussion:

DF is more common in children and adults than old age persons. The mosquito bites during day time. The children and adults are more mobile than old age persons and hence more likely to be bitten. Female: male sex ratio is 1.1:1, it suggests nearly equal sex distribution. 70% cases of DF were recorded between September to December 2014 (monsoon season) as compared to the 30% cases of DF which were recorded between January to August 2014, during winter and summer season. It suggests DF is more in monsoon season as more water pits are formed in monsoon season for breeding of mosquitoes.As shown in table 1, clinically fever was a presenting symptom 97.2% cases, followed by muscle pain in 87.3%, vomiting in 78.8%, and skin rash in 1.4% cases. The skin rashes are a rare feature in primary DF but are common in secondary DF or DHF. Laboratory profiles suggest that thrombocytopenia and leucopoenia may be due to direct suppression of bone marrow by DF virus. Anaemia is due to poor nutritional status of the affected community. Our results are comparable with studies as shown in table 1. Elevated SGPT levels were noted in 3 cases (4.1%). Pleural effusion and ascites were detected by ultrasonography only in 4 cases (5.8%).

The studied community was exposed to primary infection, so its clinical complications such as DHF and DSS were not detected. The secondary DF is usually associated with DENV2 virus subtype infection followed by second DENV2 virus subtype infection within 2-5 or up to 20 years after primary DF infection.[8] Deaths were noted in 3(4.2%) cases. 2 cases out of 3 cases were associated with fatal end stage diseases, chronic liver disease with portal hypertension, while 1(1.4%) case was associated with falciparum malaria and multiple organ dysfunction syndrome. The associated diseases were diagnosed in 28 cases(39.4%) i.e. respiratory disease in 6 cases (8.4%); enteric fever, acute viral hepatitis & falciparum malaria in 4 cases each (5.6%); chronic liver disease in 3 cases(4.2%); tuberculous meningitis with lymphadenopathy, systemic lupus erythromatosis and urinary tract infection in 1 case each (1.4%). All were mere coincidental clinical diseases. The associated enteric fever and malaria cases suggest associated seasonal infection in the studied community. The symptomatic treatment was main stay of therapy. The dehydration in patients was corrected by average 10.6 drips/ patient during hospitalisation and 2.6 drips/patient/day. [9] The antibiotic therapy was started in 37 (52.2%) cases initially but antibiotic was discontinued in most of the cases except when it was indicated for associated infective disease i.e. enteric fever or acute exacerbation of COPD. The antimalarial therapy was advised in 15 (21.2%) cases while malarial parasites detected in 9 (12.6%) cases. The data suggests the reasonable use of antimalarial therapy on clinical judgment initially but it was discontinued when malarial parasites were not detected in blood smear examination.

Conclusion:

High grade fever, muscle pain, and vomiting were main clinical symptoms while skin rashes and haemorrhagic manifestations ware rare manifestations of primary DF. Leucopoenia and thrombocytopenia detected as common laboratory finding. Abnormal LFT, pleural effusion and ascites were rare manifestations of primary DF. DHF and DSS were noted as a rare complication of primary DF. Symptomatic therapy and management of associated disease was more important as mortality depends more on associated disease. Common associated infective diseases include enteric fever, malaria and respiratory diseases.

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