

Hematological and Coagulation Profile in Dengue Cases Admitted at Tertiary Care Hospital

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Abstract

Background: Dengue is one of the important public health problems in India. The main laboratory abnormalities found in dengue are thrombocytopenia, leukopenia, haemoconcentration & derangement of coagulation profile.

Aim and objective: To study haematological and coagulation profile in dengue cases admitted at tertiary care hospital, Gujarat.

Materials and Methods: This is an observational study of 74 (M - 44, F - 30) cases with diagnosis of dengue for period of one year. Data taken from patient's blood sample sent for routine investigation at haematology & microbiology laboratory. Reading of haematological and coagulation profile were collected, compiled and analysed.

Result: Majority of case 48.65% having dengue infection belong to the age group of 15 - 30 years. Thrombocytopenia was found in 71.62% patients, leukopenia in 39.18% patients and low haematocrit value in 67.56% patients. High MPV observed in 40.54% cases and high MPDW observed in 44.59% cases. Prolonged PT and aPTT observed in 71.62% and 27.03% cases respectively and elevated D - dimer observed in 74.32% cases.

Conclusion: The result showed that increasing severity of thrombocytopenia and leukopenia associated with advanced clinical spectrum. Haematocrit, MPV and MPDW are variable with different clinical spectrum of dengue. So, correlation of deranged coagulation parameter like D - Dimer, PT and aPTT can be used as markers for predicting more severe forms of clinical spectrum of dengue.

Keywords: classical dengue fever (CDF); dengue haemorrhagic fever (DHF); dengue shock syndrome (DSS); thrombocytopenia

Introduction

Dengue is the most extensively spread mosquito - borne disease, transmitted through the bite of infected mosquitoes of *Aedes* species [1]. Dengue is caused by one of the four serotypes of the dengue virus (DEN-1, DEN-2, DEN-3 and DEN-4) also referred as an arbovirus (arthropod - borne viruses) that belongs to the genus Flavivirus of the family Flaviviridae [2]. It is a disease with a wide clinical spectrum and a wide variety of presentations, ranging from asymptomatic to an undifferentiated fever (viral syndrome) to the more severe forms such as severe dengue (SD) or Dengue haemorrhagic fever (DHF) [2]. The CDF is classically a self - limiting, nonspecific illness characterized by fever, headache, myalgia, and constitutional symptoms. DHF is a more serious clinical entity [2]. The WHO classifies DHF in four grades (I to IV). The DHF grades I and II represent relatively mild cases without shock, whereas grade III and IV cases are more severe and accompanied by shock [2]. Although CDF is a self - limited febrile illness, DHF is characterized by prominent haemorrhagic

manifestations with thrombocytopenia, increased vascular permeability, and is associated with a high mortality rate. The primary pathophysiologic abnormality seen in DHF is an acute increase in vascular permeability that leads to plasma leakage into the extravascular compartment. [2] The WHO defines dengue shock syndrome (DSS) as DHF plus signs of circulatory failure manifested by rapid and weak pulse, narrow pulse pressure (20 mmHg) or hypotension for age, prolonged capillary refill, cold and clammy skin, and restlessness [2]. Initial infection with a particular serotype (the primary infection) is usually asymptomatic or results in mild disease manifestations. However, subsequent infection (secondary dengue infections) may lead to severe disease which manifests in the form of DHF/DSS [2]. The haematological effects observed are changes in blood counts, haemoconcentration due to plasma leakage, leucopenia because of decreased neutrophils near the end of the febrile phase, presence of atypical lymphocytes and relative lymphocytosis before shock, thrombocytopenia and changes in blood haemostasis with frequent presence of haemorrhagic manifestations [3]. Among laboratory tests, both non - specific [Complete blood count, prothrombin time (PT), activated partial thromboplastin time (aPTT)] and specific tests (serology for antibody examination) are used [2]. So, the present study aimed to assess the haematological dynamics of patients with dengue fever in order to increase the sensitivity of the screening by healthcare professionals in the most serious cases and try to identify laboratory markers that may indicate the severity and outcome of disease.

Materials and Methods

The study was conducted in dengue NS1Ag and IgM positive patients, hospitalised at Sir Takhtasinhji General Hospital, Bhavnagar after getting permission from Institutional Review Board.

Inclusion Criteria

Hospitalised cases of dengue NS1 antigen and Ig M positive cases.

Exclusion Criteria

Other conditions associated with dengue which include similar haematological changes like ITP, Aplastic anaemia, infections leading to thrombocytopenia, bone marrow failure, cancer, exposure to radiotherapy etc. Drugs affecting the haematological profile and coagulation profile like warfarin, heparin, antiplatelet drugs, anticancer drug etc.

Study Type

Cross - sectional observational study of 74 cases for period of one year.

Sample Collection

Data taken from dengue patient's blood sample sent for routine investigation at central pathology and microbiology laboratory of Sir Takhtasinhji General Hospital, Bhavnagar.

Test Method

1. NS1Ag and IgM Ab done by ELISA. 2. Complete blood count by automated haematology analyser and confirmed by peripheral smear examination. 3. PT, aPTT and D - dimer by automated coagulometer 4. ESR done by semiautomated ESR machine 5. CRP done by latex agglutination method

Statistical Analysis

All data collected & entered in Microsoft Office Excel and statistical analysis was done.

Results

In this study, clinical spectrum of dengue having 45 (60.81%), 24 (32.43%) and 5 (6.75%) cases of CDF, DHF and DSS respectively. Majority, 48.65% cases are belonging to the age group of 15 - 30 years of age which includes 60% cases of DSS, 50% cases of DHF and 46.66% cases of CDF. Anaemia observed in 31 (56.36%) patients. Among them, 12 (37.5%)

were male & 19 (82.60%) were female. Degree of anaemias more common in female as compared to male. Leukopenia observed in 29 (39.18%) cases as well as leucocytosis in 11 (14.86%) cases. Maximum cases of leukopenia observed in DSS followed by DHF, which is 5 (100%) cases and 13 (54.17%) cases respectively.

Table 1: Frequency distribution of important haematological indices (Total leucocyte count).

| TLC (4000 - 11000) cells/cumm | CDF (n - 45) | DHF (n - 24) | DSS (n - 5) | Total (n - 74) |
|-------------------------------|--------------|--------------|-------------|----------------|
| <4000 | 11 (24.44%) | 13 (54.17%) | 5 (100%) | 29 (39.18%) |
| 4001 - 11000 | 26 (57.78%) | 8 (33.33%) | 0 | 34 (45.94%) |
| >11001 | 8 (17.78%) | 3 (12.5%) | 0 | 11 (14.86%) |

Total 53 (71.62%) cases of thrombocytopenia observed out of these maximum 28 (37.84%) cases having moderate thrombocytopenia. In DSS, severe thrombocytopenia observed in majority 3 (60%) cases where as in DHF and CDF, 16 (66.66%) cases and 10 (22.22%) cases showing moderate thrombocytopenia.

Table 2: Frequency distribution of important haematological indices (Platelet count).

| Platelet count (150000 - 450000) cells/cumm | CDF n - 45 (%) | DHF n - 24 (%) | DSS n - 5 (%) | Total (n - 74) |
|---|----------------|----------------|---------------|----------------|
| <20000 | 1 (2.22%) | 3 (12.5%) | 3 (60%) | 7 (9.46%) |
| 20001 - 60000 | 10 (22.22%) | 16 (66.66%) | 2 (40%) | 28 (37.84%) |
| 60001 - 100000 | 7 (15.55%) | 5 (20.83%) | 0 | 12 (16.22%) |
| 100001 - 150000 | 6 (13.33%) | 0 | 0 | 6 (8.11%) |
| >150001 | 21 (46.67%) | 0 | 0 | 21 (28.37%) |

Low haematocrit observed in total 50 (67.56%) cases which includes 4 (80%) cases of DSS, followed by 33 (73.33%) cases of CDF and 13 (54.17%) cases of DHF.

Table 3: Frequency distribution of important haematological indices (Haematocrit).

| PCV (38 - 45) % | CDF n - 45 (%) | DHF n - 24 (%) | DSS n - 5 (%) | Total n - 74 (%) |
|-----------------|----------------|----------------|---------------|------------------|
| <38.0 | 33 (73.33%) | 13 (54.17%) | 4 (80%) | 50 (67.56%) |
| 38.1 - 41.0 | 3 (6.67%) | 8 (33.33%) | 0 | 11 (14.86%) |
| 41.1 - 45.0 | 7 (15.55%) | 3 (12.5%) | 0 | 10 (13.51%) |
| >45.01 | 2 (4.44%) | 0 | 1 (20%) | 3 (4.05%) |

High MPV observed in 30 (40.54%) cases, this includes 3 (60%) cases of DSS, 20 (44.44%) cases of CDF and 7 (29.17%) cases of DHF. High MPDW observed in 33 (44.59%) cases which includes 4 (80%) cases of DSS, 15 (62.5%) cases of DHF and 14 (31.11%) cases of CDF. Total 53 (71.62%) cases having prolonged prothrombin time. From which 34 (75.56%), 17 (70.83%) and 2 (40%) cases of CDF, DHF and DSS respectively. Prolonged aPTT observed in 20 (27.03%) cases out of these 14 (31.11%) cases of CDF followed by 5 (20.83%) cases and 1 (20%) case of DHF and DSS showing prolonged aPTT respectively. Total 55 (74.32%) cases having high D - dimer value. In DSS and DHF, 100% cases observed with high D - Dimer value whereas only 26 cases of CDF (57.78%) having elevated D - dimer value.

Table 4: D-dimer value in dengue cases.

| Studies | Number of cases with elevated D - dimer value | | | |
|---------------------------|---|-------------|-----------|---------------|
| | CDF (%) | DHF (%) | DSS (%) | Total (%) |
| Present study | 26/45 (57.78) | 24/24 (100) | 5/5 (100) | 55/74 (74.32) |
| Kumari et al [5] | 20 (23.5) | 7 (63.60) | 4 (100) | 31 (31) |
| K. Setkrasing, et al [18] | 4 (13) | 26 (87) | - | 30 (73.17) |

CRP positive in 46 (62.16%) cases. Normal ESR observed in 44 (59.45%) cases, which includes 30 (66.67%) cases of CDF, 13 (54.17%) cases of DHF and 1 (20%) case of DSS. Lymphocytosis observed in 21 (38.37%) cases which includes 2 (40%) cases of DSS, 8 (33.33%) cases of DHF and 11 (24.44%) cases of CDF. Lymphopenia observed in 11 (14.86%) cases which includes 9 (20%) cases of CDF and 2 (2.33%) cases of DHF. Neutropenia observed in 10 (13.51%) cases from which 2 (40%) cases of DSS, 3 (12.5%) cases of DHF and 5 (11.11%) cases of CDF. Eosinophilia was observed in 6 (8.10%) cases which includes 4 (8.88%) cases of CDF and 2 (8.33%) cases of DHF. No significant changes observed in monocyte and basophil count. The most common change in haematology parameter is elevated D - dimer value in 55 (74.32%) cases followed by thrombocytopenia, leukopenia & prolonged prothrombin time in 53 (71.62%) cases along with high MPV in 30 (40.54%).

Discussion

In this study, clinical spectrum of dengue having 60.81%, 32.43% and 6.75% cases of CDF, DHF and DSS respectively. Studies conducted by Meena KC et al [4] and Kumari et al [5] also observed majority cases having clinical spectrum of CDF followed by DHF then DSS. In present study, majority of the cases 48.65% (n - 36) are belonging to the age group of 15 - 30 years of age. A similar result observed in study conducted by Meena KC et al [4] and Navya B N et al [6] shows the age of the patient in their study was 21 - 30 years and 21 - 40 years of age respectively. This may be due to young adults are being more active outside from the home [4]. In present study, we observed male is affected more than female. This result is similar with the study conducted by Meena KC et al [4] and Joshi AA et al [7]. This is because males are more prone to exposed than females because of their outdoor life which they lead. Further, female in India is usually better clothed than males, hence they are less exposed [4]. In present study, we observed anaemia in 56.36% cases while studies conducted by Meena KC et al [4] and Patel K et al [8] observed anaemia in 4% and 12.30% cases respectively.

In present study, Leukopenia is observed in 39.19% cases and leucocytosis observed in 14.86% cases. Which is in accordance with the study conducted by Meena KC et al [4], Joshi AA et al [7], Patel K et al [8]. Leukopenia is because of direct bone marrow suppression by virus [8]. From the pathophysiological point of view, leucocytosis indicates a superimposing bacterial infection and/or other stressful stimuli [9]. In present study, we observed 71.62% cases having thrombocytopenia which is consistent finding with the studies conducted by Meena Kc et al [4], Navya B.N et al [5] and many other studies [7, 9, 10].

In present study, Low haematocrit is observed in 67.56% cases while other studies by Meena KC et al [4], Kumari et al [5] and Patel K et al [8] observed 54% cases, 75% cases and 24.61% cases with low haematocrit respectively. Reason for the low haematocrit is may be either because of anaemia or patient receiving i.v. fluid therapy [4]. Decreased HCT in an unstable patient may indicate bleeding and act as a predictor for red cell transfusions, whereas it suggests recovery from disease in a stable patient [10]. In present study, we observed majority cases 48.64% having normal MPV and low MPV in only 10.81% cases. However, studies conducted by Navya B.N et al [6], Kantharaj A [10], Muddappu et al [11] and Mukker P et al [12] observed low MPV because in their studies they compare the data with severity of disease while we use the random single sample for data. MPV indicate platelet function and bone marrow activity; a high MPV indicates increased megakaryocyte activity. A low MPV indicates marrow suppression and increased risk of bleeding [6].

In present study, we observed majority cases (44.59%) having high MPDW. This result is concordance with studies conducted by Navya B.N et al [6] and Muddappu et al [11], which is 67.61% cases and 92% cases respectively. Platelets with increased number and size of pseudopodia differ in size, possibly affecting platelet distribution width (PDW) which increases during platelet activation [11]. In present study, we observed prolonged PT in 71.62% cases. which is accordance with the studies conducted by Pranesh [13], Joshi R, et al [14] and Bashir BA et al [15]. While studies conducted by Kannan A et al [16] and GR Patel et al [17] shows majority cases with normal Prothrombin time.

In present study, we observed 72.97% cases having normal aPTT value. Similar results are observed in study conducted by Pranesh [13] and Kannan a et al [16] which are 57% and 77.7% respectively. Prolongation of PT and aPTT might be caused either by the downregulation of synthesis of specific factors or by an increase in consumption of specific factors [17]. Our study shows consistently higher D - dimer levels in all cases of DHF and DSS patients compared to CDF patients which is comparable with other studies by Kumari et al [9] and K. Setrkrasing, et al [18]. In present study, 62.16% cases are CRP positive while Kumari et al [5] observed only 30% cases were CRP positive. High CRP indicates the severity of the disease. similar results also observed in other studies conducted by Chen CC et al [19], R Rao et al [20] and Aaradhana et al [21].

In present study, 40.54% cases having high ESR whereas study conducted by Kumari et al [5] and Souza LJ et al [21] showing 10% and 21.34% cases with high ESR respectively. In Present study, we observed lymphocytosis in 38.37% cases while 30% and 65% cases show lymphocytosis in study conducted by Kumari et al [5] and Joshi AA et al [7] respectively. 14.86% cases having lymphopenia in present study while only 2% cases showing lymphopenia in study conducted by Kumari et al [6].

In present study, we observed 13.51% cases of neutropenia and 1.35% cases of neutrophilia. This result is similar with study conducted by Kumari et al [5] and Joshi AA et al [7]. In present study eosinophilia is observed in 8.10% cases while study conducted by Joshi AA et al [7] observed eosinophilia in 5% cases. Sushma Nayar et al [22] observed that eosinopenia was seen in the acute phase of the disease and a rebound increase in eosinophils was seen with an increase in absolute eosinophil count in recovery phase.

Limitations of this study

- Smaller study size. • No follow up of cases included in the study. • Haematology and coagulation parameters were not analysed separately in different phases of dengue. Therefore, the exact pattern of abnormalities prevalent in patients with dengue at different stages may not have been observed in the study.

Conclusion

This study is conducted on 74 cases of dengue infected patients with different clinical spectrum admitted at Sir Takhtasinhji general hospital, Bhavnagar, Gujarat. Leucopenia and thrombocytopenia are significant findings observed in our study. Leucopenia is associated with lymphocytosis. Anaemia is observed in most of the cases of all spectrum of dengue. Haematocrit, MPV and MPDW are variable with different clinical spectrum of dengue. Correlation of deranged coagulation profile like D - Dimer, PT and aPTT with severity of disease predict the Progression and outcome of disease.

Abbreviations: CDF: Classical dengue fever

DHF: Dengue haemorrhagic fever

DSS: Dengue shock syndrome

PT: Prothrombin time

aPTT: Activated partial thromboplastin time

MPV: Mean platelet volume

MPDW: Mean platelet distribution width

CRP: C-reactive protein

ESR: Erythrocyte sedimentation rate

NS1Ag: Non-structural protein 1 antigen

IgM Ab: Immunoglobulin M antibody

ELISA: Enzyme-linked immunosorbent assay

WHO: World Health Organization

SD: Severe dengue

HCT: Haematocrit

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