Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 03, 2024

STUDY OF CLINICAL PROFILE AND ROLE OF HEMATOLOGICAL MARKERS IN PROGNOSIS OF DENGUE FEVER AT TERTIARY CARE HOSPITAL, KIMS, KOPPAL

Anand Chavan[1], Dhanya K[2], Umesh Rajoor[3], Gavisiddesh[4]

[1]Assistant Professor, Department of General Medicine, KIMS, Koppal
[2]Assistant Professor, Department of Pathology, KIMS, Koppal
[3]Professor and head, Department of General Medicine, KIMS, Koppal
[4]Assistant Professor, Department of General Medicine, KIMS, Koppal

Corresponding author :Dr Gavisiddesh, Assistant Professor, Department of General medicine, KIMS, Koppal

ABSTRACT

Introduction: Dengue is the most common insect-transmitted viral disease in the world having Adesaegypti mosquito as their principal vector.Initial dengue infection may be asymptomatic with nonspecific febrile illness. While most patients recover following a self-limiting non-severe clinical course, a small proportion progress to severe disease characterized by plasma leakage with or without dengue hemorrhagic fever (DHF). Peripheral blood parameters change during the course of the illness in the form of rising Hematocrit, changing hemoglobin, leucopenia, atypical lymphocytes, thrombocytopenia and altered LFT. A rapid decrease in platelet count, concomitant with a rising Hematocrit, is suggestive of progression to plasma leakage.

Objectives: The purpose of this research was to examine the dengue patients for clinical features and correlate them with day wise changes in hematological parameters thus, identifying the factors contributing to severe dengue to help guide individuals toward early prevention of complications.

Methodology: We prospectively analyzed the hematological findings of patients admitted with dengue viral infection from March 2022 to March 2023. Dynamic profile of hematological parameters in severe and non-severe patients was analyzed at different time points after admission, and correlated with patient outcome.

Results: There were total 87 cases with male to female ratio of 1:1.02. Majority of the patients, 79 cases(90.80%) presented with fever, headache and malaise followed by multiple joints pain, abdominal pain, giddiness, nausea, vomiting, throat pain and loose stools. Bleeding manifestations were seen in 2 patients(2.29%). A total of 12 cases(13.79%) showed features of severe dengue like hemoglobin level > 15 g/dl, rise in haematocrit >20% on successive day, altered leukocyte count, atypical lymphocytes, thrombocytopenia and altered Liver function tests. Elevated transaminases were seen in 52.87% and raised bilirubin levels in 24.13%. Jaundice was observed in 100% of severe dengue cases

Conclusion: Identification of warning signs of severe dengue and appropriate clinical management are key elements of care to prevent the progression of disease and mortality.

Keywords: Dengue fever, plasma leakage, thrombocytopenia,hematocrit.

INTRODUCTION:

Dengue virus (DENV) is the most common insect-transmitted virus in the world, causing symptoms ranging from none to serious systemic illness or "break bone" fever (severe fever and pain) [1]. Over 5 million cases and over 5000 dengue-related deaths have been reported from 86 countries/territories globally[2]. Mortality rates are 10–20% and if dengue shock syndrome develops, mortality rates can reach up to 40%.[1]

Dengue disease begins after an incubation period of 4–7 days, typically patient experiences sudden onset of fever, frontal headache, retro orbital pain, and back pain along with severe myalgia. These symptoms gave rise to the colloquial designation of dengue as "break-bone fever." [1]

DENV has four serotypes (DENV-1, DENV-2, DENV-3, DENV-4). All four viruses have Ades aegypti mosquito as their principal vector.Infection with one serotype provides long-term immunity to the same serotype and only transient immunity to the other serotypes, after which secondary infections with a different serotype increase the risk for developing severe dengue.

Initial dengue infection may be asymptomatic (50-90%), may result in a nonspecific febrile illness, or may produce the symptom complex of classic dengue fever (DF). Classic dengue fever is marked by rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone),weakness, vomiting or sore throat. While most patients recover following a self-limiting non-severe clinical course, a small proportion progress to severe disease, mostly characterized by plasma leakage with or without dengue hemorrhagic fever (DHF) [2]. Severe dengue may involve shock, severe bleeding or severe organ impairment. This stage often starts after the fever has gone away and it is preceded by warning signs such as intense abdominal pain, persistent vomiting, bleeding gums, fluid accumulation, lethargy or restlessness, and liver enlargement.[2]

WHO classification of dengue based on severity[3]

1. Dengue without warning signs

2. Dengue with warning signs (abdominal pain, persistent vomiting, mucosal bleeding, fluid accumulatin, liver enlargement, lethargy, postural hypotension, raised Haematocrit with rapid decrease in platelet count)

3. Severe Dengue (severe plasma leakage, hemorrhage, organ impairment)

The diagnosis is made by IgM antibody detection by ELISA method or by NS1 antigen-detection or paired serology during recovery or by RT-PCR method during the acute phase. Virus is readily isolated from blood in the acute phase if mosquito inoculation or mosquito cell culture is used[1].

Clinical course of dengue hemorrhagic fever consists of three stages[3, 4],
Febrile phase (lasting 2–7 days)
Critical phase (Leaking phase) (24–48 h)
Convalescent phase (2–4 days)

In milder cases, restlessness, lethargy, thrombocytopenia (<1,50,000/μL), and hemoconcentration are detected 2–5 days after the onset of dengue fever. Severe dengue is identified by the detection of bleeding tendencies (tourniquet test, petechiae).

Peripheral blood parameters change during the course of illness. Dengue fever is characterized by leucopenia (White Blood Cells < 4000 cells/mm3), thrombocytopenia (< 1,50,000 cells/μL), rising haematocrit levels (5–10%) and there should be no evidence of plasma leakage[4]. A rapid decrease in platelet count, concomitant with a rising haematocrit, is suggestive of progression to plasma leakage.
Lymphocytosis especially atypical lymphocytosis and neutropenia are the consistent findings.[5]
Liver function tests also show altered parameters as the disease progresses.

Shock may result from increased vascular permeability. In more severe cases, frank shock is apparent with low pulse pressure, cyanosis, hepatomegaly, pleural effusions, and Ascites. In some patients, severe ecchymoses and gastrointestinal bleeding develop. The period of shock lasts only 1 or 2 days[1].

There is no specific treatment for dengue, but the timely diagnosis of cases, identification of warning signs for severe dengue, and appropriate clinical management are key elements of care to prevent the progression of disease to severe dengue and deaths. Typing and cross matching of blood should be performed if there is development of warning signs, as blood products may be required in the course of treatment.

Objectives:

1. To study the clinical presentation of dengue cases.
2. To study daywise hematologicalparameters of patients duringtheir disease course.
3. To correlate the changing pattern of these hematological parameters with clinical outcome of the patient.

Methodology

A prospective observational study was done among patients admitted to tertiary care hospital with dengue virus infection to know the early clinical and laboratory predictors ofsevere dengue. Ethical clearance was obtained from the institutionalethicalreviewcommittee. Patients who got admittedtoourhospital with suspected Dengue fever fromMarch 2022 to March 2023, were subjected to serological tests like detection of Dengue specific IgM and IgG

using ELISA method. Only seropositive cases were included in the study. Data was collected in a prewritten proforma. Details of the cases like serial day wise clinical findings, laboratory findings and outcome were recorded in patient data sheet.

3 cc of blood samples were drawn inEDTA tube for testing the Complete Blood counts (CBC) atthetimeofadmissionandserially up to last day of hospital stay. CBC testing was done using EDAN 5 part analyzer.Peripheral blood smears were stained using Field's A and B stains and differential counts were performed to determine the percentages of different leukocytes. Platelet counts were recorded in each individual and the results were verified on peripheral smear study.

Since defervescence occurs around day 3,for statistical analysis Laboratory values on day 3 were considered and difference of values on successive day were studied. These changing parameters helped in identifying the warning signs and prevent progression of disease to critical phase. Medications, intravenous fluids and blood components were administered accordingly. Subjects were discharged from the hospital if they were clinicallystable and afebrile for at least 24 hours.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using Epi Info 7.2.6 version software [CDC]. Categorical data was represented in the form of Frequencies and proportions. Normality of the continuous data, was tested by Kolmogorov–Smirnov test and the Shapiro–Wilk test.

Results

A total of 87 cases were included in our study, of which 44 were females and 43 were males. Male to Female ratio was 1:1.02. Age of patients ranged from 16 years to 66 years. Mean age of the patients was 30.53 years. Majority of the patients, 79cases(90.80%) presented with fever, headache and malaise. Second most common symptom was multiple joints pain seen in 10 cases(11.49%) followed by abdominal pain in 9 cases(10.34%), giddiness, nausea and vomiting in 8 cases(9.19%). Few patients presented with atypical symptoms like cough and throat pain observed in 4 cases(4.59%) and loose stools in 3cases(3.44%). Bleeding manifestations were seen in 2 patients(2.29%), that is haematuria in one patient and oral bleeding in other patient. There was a single case(1.14%) who presented with altered sensorium to the emergency department(Table 1). A total of 12 cases(13.79%) showed features that could fit into the WHO category of dengue fever with warning signs (Table 2).

There was one patient with cirrhosis of liver who was a known case of Hepatitis B and another case showed renal impairment due to preexisting cystitis and pyelonephritis. None ofthe patients showed signs and symptoms of Dengue Shock Syndrome. No mortality was observed in present study.

Table 1: Clinical symptoms in admitted Dengue cases

Mode of presentation	Number of cases	Percentage
Fever	79	90.80%
Multiple joints pain	10	11.49%
Abdominal pain	9	10.34%
Giddiness	8	9.19%
Nausea, vomiting	8	9.19%
Cough, throat pain	4	4.59%
Loose stools	3	3.44%
Bleeding manifestation	2	2.29%
Altered Sensorium	1	1.14%

Table 2: WHO categories of Dengue cases

WHO category	Number of cases	Percentage
Dengue without warning signs	75	86.20%
Dengue with warning signs	12	13.79%

CBC parameters were assessed on daily basis and day 3 investigation findings were used to detect warning signs for development of severe dengue(Table 3).

Hemoglobin values were ranging from 3.4-16.9 g/dl with a mean value of 12.72 g/dl. 18 cases(20.68%) had hemoglobin level of more than 15 g/dl.

Haematocrit values ranged from 18.6% to 56.3%. Mean Hematocrit value was 27.4%. A rise in haematocrit >20% on successive day was seen in 5 cases(5.74%).

Table 3: Warning signs of severe Dengue

Lab investigation	Warning sign	Number of cases	Percentage
Hemoglobin	>15g/dl	18	20.68%
Haematocrit	>20% rise on next day	5	5.74%
Leukocytes	<4,000/dl	17	19.54%
	>11,000/dl	1	1.14%
Lymphocyte count	>45%	43	49.42%
Atypical lymphocytes	Present	31	35.6%
Platelets	<1,50,000	75	86.2%

We observed that 17 cases(19.54%) had leucopenia(<4000), 69 cases(77.01%) had normal WBC counts (4,000-11,000) and only 1 case(1.14%) showed leucocytosis(>11,000). High lymphocyte count (>45% differential lymphocyte count) was seen in 43 cases(49.42%) and on peripheral smear examination, atypical lymphocytes were seen in 31 cases(35.6%).

In our study we divided patients into 4 groups based on mean platelet counts. Group1-severe thrombocytopenia (<20,000/micro liter), Group2- moderate thrombocytopenia(21,000-50,000/micro liter), Group3- mild thrombocytopenia(51,000- 1,50,000/micro liter) and Group4-normal platelet count(1,50,000- 4,00,000/micro liter). Thrombocytopenia(<1,50,000/micro liter) was seen in total of 75 cases**(**86.2**%).**

Group 1 with severe thrombocytopenia comprised of 5 patients(5.74%) of which, 4cases(80%) had signs and symptoms of dengue hemorrhagic fever. Group 2 had 26 patients(29.88%) with moderate thrombocytopenia of which 7 cases(26.92%) showed features of DHF. Group 3 with mild thrombocytopenia consisted of 44 cases(50.57%) of which, 1 case presented with DHF and group 4 with normal platelet counts consisted of 12 cases(13.79%). None among group 4 had severe dengue features.[Table 4].

Table 4: Mean platelet count and outcome of patient.

Group	Mean platelet count/ micro liter	Number of cases	Percentage of cases with DHF
1	<20,000	5	80%
2	21,000-50,000	26	26.92%
3	51,000- 1,50,000	44	2.27%
4	1,50,000- 4,00,000	12	-

A diagnosis of DHF was made if there was presence of thrombocytopenia, increase in haematocrit level >20% of previous day value, and evidence of plasma leakage like pleural effusion/ascites. There were 12 such cases (13.79%) with above mentioned features.

DISCUSSION:

Dengue infection presents commonly as fever, characterized by a downward trend in temperature over the period of time. A peak in the plasma viral RNA levels is seen which decreases to undetectable levels by 7th day of fever. Thus the downward trends in viral RNA level and body temperature are in correlation with each other[6]

In our study, fever was the most common presenting symptom seen in 90.80% cases which is in accordance with study findings by Jameel T et al[7]and Tewari K et al[8]who also observed fever as the commonest symptom seen in 98% and 99.8% of their patients respectively.

Hemoconcentration is a well-known finding of DHF[3.4] .Increased Hematocrit level secondary to plasma extravasation or third-space fluid loss leads to hemoconcentration and thus increased hemoglobin levels. In our study the hemoglobin levels among patients ranged from 3.4-16.9 g/dl with a mean of 12.72 g/dl. 12cases(21.14%) which were categorized as severe dengue had a hemoglobin level of more than 15 g/dl between day 3 and day 7 . Similar findings were shown in study by ChaloemwongJ et al[9] where higher hemoglobin and hematocritvalues were found significantly on day 3 to day 10 (highest on day7). Study by Abija Babuji[10] showed mean Hemoglobin value of 12.72 g/dl and 21.14% cases in their study had a hemoglobin level of more than 15 g/dl. Ralapanawa U et al[11] showed significantly higher hemoglobin values among leakers compared to non-leakers.

When plasma leakage through the blood vessels occur,Hematocrit value is expected to rise[3,4,12].Haematocrit(HCT) monitoring is used to evaluate the degree of plasma leakage and to determine the mode of intervention. If a dengue patient has a persistently high haematocrit with unstable vital signs, this indicates active plasma leakage and the need for further fluid replacement therapy.

In present study, Hematocrit levels had decreasing trend with a range of 18.6% – 56.3%. Mean Hematocrit value was 27.4% . A rise in haematocrit >20% was seen only in 5 cases(5.74%). This is in contrast to findings of studies by ChaloemwongJ et al[9] and Nandwani et al[13] who observed an increasing haematocrit levels of > 20% in >40% cases. However study by Kadadavar et al[14] who also noticed low hematocrit values in most of their cases, attributed it to the increasing prevelance of anemia in their region. Since automated cell counters calculate the hematocrit value by multiplying red blood cell number (in millions/mm^3) by the mean corpuscular volume (MCV, in femtoliters),accurate measurement of the MCV is necessary[15] .Similar influencing factor was observed in our study as ours is a region with increasing cases of microcytic hypochromic anemia(low MCV) which indirectly reduces haematocrit values .

Leucocytes are expected to decrease in number in dengue fever. Any change in the values of total leukocyte count suggests progression of the disease towards severity.In our study, 17 cases(19.54%) had leucopenia(<4000) which gradually improved around 5^{th} day of disease. 69 cases(77.01%) showed leukocyte counts within normal range (4,000-11,000) and only 1 case(1.14%) showed leukocytosis(>11,000). Similar findings were recorded in study by ChaloemwongJ etal[9] in which leucopenia was found in 30.8% cases from day 2 of fever and the incidence increased on successive days of the fever until day 5 when 78.8% cases had leucopenia.

In present study we found that Lymphocyte counts were relatively high in 43 cases(49.42%). In study done by Rao A et al[16]thepercentage of lymphocytes in the differential leukocyte count at the time of admission showed a significantnegative correlation with the duration of hospital stay.On peripheral smear examination, we found that 31 cases(35.63%) had atypical lymphocytes of which 12 cases already had signs and symptoms of severe dengue. Clarice et al[17] also noticed that severe dengue cases had a significantly higher percentage of atypical lymphocytes compared to dengue cases without

warning signs and a significant negative association between platelet counts and atypical lymphocyte countswere noted.

Evidence suggests that DENV can induce bone marrow hypoplasia during acute phase of the disease[18] . Thrombocytopenia in dengue may arise either from decreased production of the bone marrow cells or from increased peripheral destruction of platelets.

In our study, thrombocytopenia was seen in 75 cases(86.2%) of which, Group 1(<20,000) comprised of 5 patients, group2(21,000-50,000) had 26 patients, group 3(51,000-1,50,000)consisted of 44 patients and group 4with normal platelet counts(>1,50,000) consisted of 12 cases. Studies done by Kadadavar et al[14] and Joshi AA et al [19] noticed thrombocytopenia in >90% of cases.

Lam PK et al[5] observed progressive reduction of plateletcountsbetweendays2and6ofillness and showed that a dailyplateletcountcanbehelpfulfor predicting progression of disease but the prognosticrelevance will be time-limited as significant reduction in platelet count was seen only 1 day prior to development of Dengue shock syndrome in their study.

Platelets are activated in patients with dengue. In a study done by Ojha et al[20] it was observed that low platelet counts coexisted with high platelet activation and vice versa during different days of infection in dengue patients. Activated platelets mediate inflammatory and immune responses using a variety of mechanisms, including release of stored cytokines and synthesis of IL-1β[21,22,23]. These factors contribute to the development of increased vascular permeability and hemoconcentration during dengue illness[21]

In present study, we noticed similar relationship between platelet counts and patient outcome. Severe dengue cases with longer duration of hospital stay were present in group 1 and 2 that is cases with severe and moderate thrombocytopenia respectively. Whereaspatients from group 3 and 4 had relatively less duration of hospital stay except one case from group 3 who developed features of DHF, thus supporting the fact that speedy recovery is seen in patients with normal or near normal platelet counts.

Clinical and experimental observations suggest that there is liver involvement during dengue infection. This liver dysfunction could be a direct viral effect on liver cells or an adverse consequence of dysregulated host immune responses against the virus[24]. Liver dysfunction varies from mild injury with elevation of transaminases to severe hepatocyte injury, resulting in jaundice[25]. Thus studying LFT in dengue patients will help in assessing the severity of disease. In our study, elevated transaminases were seen in 46 cases(52.87%) and raised bilirubin levels in 21 cases(24.13%). Jaundice was observed in 100% of severe dengue cases and 12% of cases with non severe dengue. Study by Swamy AM et al[25] showed elevated transaminase levels in 74.2% cases and hyperbilirubinemia in 9.1% of patients. Itha et al[26] reported jaundice among 15% of their study population.

Conclusion: Because of the high incidence of Dengue cases and the potential for serious complications, reviewing known antecedent features of complications is important which contributes to the reduction of mortality rates. Observation of hematological parameters for

warning signs of severe dengue and appropriate clinical management are key elements of care to prevent the progression of disease and deaths.

REFERENCES:

1. In: Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J. eds. *Harrison's Principles of Internal Medicine, 21e*. McGraw-Hill Education; 2022. [Internet] Accessed February21,2024. https://accesspharmacy.mhmedical.com/content.aspx?bookid=3095&sectionid=259856983.
2. WHO- Dengue global situation. Disease outbreak news, 21st December 2023. [Internet] Accessed February21,2024. https://www.who.int/emergencies/disease-outbreak-news/item/2023.
3. WHO.Comprehensiveguidelinesforpreventionandcontrolofdengue anddenguehaemorrhagicfever.Geneva:WHO;2011.
4. Handbook for clinical management of dengue – World Health Organization2012.[Internet] Accessed February21,2024http://www.wpro.who.int/mvp/documents/handbook_for_clinical_management_of_dengue.pdf.A
5. Lam PK, Ngoc TV, Thu Thuy TT, Hong Van NT, Nhu Thuy TT, Hoai Tam DT, et al. (2017)The value of daily platelet counts for predicting dengue shock syndrome: Results from a prospective observational study of 2301 Vietnamese children with dengue. PLoS Negl Trop Dis. 2017; 11(4): e0005498.
6. Tsai JJ, Chokephaibulkit K, Chen PC, Liu LT, Hsiao HM, Lo YC, et al. Role of cognitive parameters in dengue hemorrhagic fever and dengue shock syndrome. J Biomed Sci. 2013; 20: 88.
7. T Jameel, K Mehmood, G Mujtaba, N Choudhary, N Afzal, RF Paul. Changing haematological parameters in dengue viral infections. Journal of Ayub Medical College, Abbottabad 2012;24 (1):3-6.
8. Tewari K., Tewari V.V., Mehta R.Clinical and hematological profile of patients with dengue fever at a tertiary care hospital – an observational study. Mediterr J Hematol Infect Dis 2018, 10(1): e2018021,
9. Chaloemwong, J., Tantiworawit, A., Rattanathammethee, T. *et al.* Useful clinical features and hematological parameters for the diagnosis of dengue infection in patients with acute febrile illness: a retrospective study. *BMC Hematol* **18**, 20 (2018).
10. Abija Babuji, S. S. Inamdar. Haematological profile of dengue fever. MedicaInnovatica Jan- Jun 2020;9(1).
11. Ralapanawa, U., Alawattegama, A.T.M., Gunrathne, M. *et al.* Value of peripheral blood count for dengue severity prediction. *BMC Res Notes* **11**, 400 (2018).
12. Tee HP, How SH, Jamalludin AR, Fariz Safhan MN, Mohd Sapian M, Kuan YC, et al. Risk factors associated with development of dengue haemorrhagic fever or dengue shock syndrome in adults in Hospital Tengku Ampuan Afzan Kuantan. *Med J*

Malaysia. 2009;64(4):316–320.

13. Nandwani, S., Bhakhri, B. K., Singh, N., Rai, R., & Singh, D. K. (2021). Early hematological parameters as predictors for outcomes in children with dengue in northern India: A retrospective analysis. Rev Soc Bras Med Trop. 2021 Jan 29;54:e05192020.
14. Kadadavar S S, Lokapur V, Nadig D, Prabhu M H, Masur D, Hematological parameters in dengue fever: A study in tertiary care hospital. Indian J PatholOncol 2020;7(2):218-222.
15. Billett HH. Hemoglobin and Hematocrit. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; 1990. Chapter 151. 718-719.
16. AnandaRao A, U RR, Gosavi S, Menon S. Dengue Fever: Prognostic Insights From a Complete Blood Count. Cureus. 2020 Nov 20;12(11):e11594.
17. Clarice CSH, Abeysuriya V, de Mel S, UvinduThilakawardana B, de Mel P, de Mel C, et al. Atypical lymphocyte count correlates with the severity of dengue infection. PLoS One. 2019 ;14(5):e0215061.
18. Nakao S, Lai CJ, Young NS. Dengue virus, a flavivirus, propagates in human bone marrow progenitors and hematopoietic cell lines. Blood. 1989 Sep;74(4):1235-40.
19. Joshi AA, Divyashree BN, Gayathri BR. Hematological Parameters in Dengue: The Serological Angle A Study. *International Journal of Hematology Research* 2018; **4(1)**: 180-184
20. Ojha A, Nandi D, Batra H, Singhal R, Annarapu GK, Bhattacharyya S, et al. Platelet activation determines the severity of thrombocytopenia in dengue infection. Sci Rep. 2017 ;7(1).
21. Hottz ED, Lopes JF, Freitas C, Valls-de-Souza R, Oliveira MF, Bozza MT, et al. Platelets mediate increased endothelium permeability in dengue through NLRP3-inflammasome activation. Blood . 2013;122(20):3405–14.
22. Hottz ED, Oliveira MF, Nunes PCG, Nogueira RMR, Valls-de-Souza R, DaPoian AT, et al. Dengue induces platelet activation, mitochondrial dysfunction and cell death through mechanisms that involve DC-SIGN and caspases. J ThrombHaemost . 2013 ;11(5):951–62.
23. Weyrich AS, Lindemann S, Zimmerman GA. The evolving role of platelets in inflammation. J ThrombHaemost. 2003;1(9):1897–905.
24. Seneviratne SL, Malavige GN, de Silva HJ. Pathogenesis of liver involvement during dengue viral infections. Trans R Soc Trop Med Hyg. 2006;100(7):608–14.
25. Swamy AM, Mahesh PY, Tumkur SR. Liver function in dengue and it's correlation with disease severity: an retrospective cross-sectional observational study in a tertiary care center in Coastal India. Pan Afr Med J. 2021 Dec 23;40:261.
26. Itha S, Kashyap R, Krishnan N, Saraswat VA, Choudhuri G, Aggarwal R. Profile of liver involvement in dengue virus infection. Natl Med J India. 2005;18(3):127.