DOI: 10.7860/IJNMR/2022/58951.2365

Original Article

Paediatrics Section

Clinical and Haematological Profile of Dengue during 2021 Epidemic at a Tertiary Care Centre, Western Uttar Pradesh, India: A Cross-sectional Study

PAYAL MITTAL[1], SHEHRAZ FIROZ[2], NEETIPRIYA PANDEY[3], DIGVIJAY GHANGAS[4], SONIA BHATT[5]

ABSTRACT

Introduction: Incidence of dengue fever has significantly increased in the last few years in developing countries. Its clinical presentation may be variable in paediatrics with high-risk of complications. Dengue fever causes high mortality and morbidity at the paediatric age group.

Aim: To evaluate the clinical features and haematological parameters of dengue in paediatric cases at a tertiary care hospital.

Materials and Methods: A cross-sectional observational study was conducted in the Department of Paediatrics, FH Medical College, Agra, Uttar Pradesh, India, on patients diagnosed with dengue fever from August 2021 to November 2021. All cases were subjected to detailed clinical history, examination and relevant investigations (laboratory parameters and clinical features). Data was collected in predesigned proforma, entered in Microsoft Excel sheet and analysed.

Results: Out of 801 patients, 486 (60.67%) were males and 315 (39.33%) were females. The commonest symptoms were fever (n=779, 97.25%) followed by body pain/ arthralgia (n=700, 87.39%), flushing (n=622, 77.65%), abdominal pain (n=437, 54.55%), and vomiting (n=428, 53.43%). Highest number of cases (n=399, 49.82%), were from dengue with warning signs. Of total, 759 (94.75%) cases had thrombocytopaenia. Common complications were pleural effusion (26.8%) and ascites (11.88%). Of total, 611 (76.27%) cases got cured while 81 (10.11%) patients expired.

Conclusion: Dengue fever is more common in paediatric age group with high rate of complications and disease severity, which has high mortality rate. High clinical suspicion and early fluid management are the only measures to reduce the mortality and morbidity.

Keywords: Aspartate aminotransferase, Immunochromatographic test, Paediatrics

INTRODUCTION

The dengue virus is of the Flavi virus genus and Flaviviridae family, responsible for the vector-borne illness, dengue [1]. The four serotypes of dengue virus are DENV1, 2, 3 and 4. The primary vectors are two species of Aedes mosquitoes: *Aedes aegypti* and *Aedes albopictus* [1]. *Aedes aegypti* is the principal vector and largely responsible for large scale epidemics globally [2]. Over the last three decades, dengue has an increasing global incidence with large periodic epidemics in endemic regions [3]. According to the World Health Organisation (WHO), the number of dengue cases reported has increased eight-fold in the past two decades from 505,430 cases in 2000 to 5.2 million cases in 2019. The number of reported deaths has increased in the past two decades. Demographic shift has also been noted with an increasing distribution among paediatric age groups [4]. India being the second most populated country in the world with rapid and haphazardly expanding urban spaces, is the perfect medium for rapid transmission [5]. This has made dengue, a leading public health problem for India [6].

The WHO classifies dengue into three major categories: dengue Fever (DF), dengue with warning signs and severe dengue [7]. The average incubation period is 4-10 days with symptoms lasting 2-7 days. In 50-90% of the cases, infection is asymptomatic, however, in others, it can manifest with the symptoms of classical DF. Symptoms consist of rapid onset high fever (40°C/104°F) with diffuse body and joint pain, headache, retro-orbital pain, weakness, vomiting, sore throat, lymphadenopathy and a centrifugal maculopapular rash among others [8]. Fever, along with any two of the above mentioned symptoms should be suspected to be dengue fever. Warning signs include: severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, fatigue, restlessness and blood in vomitus [9]. Patients who present with bleeding manifestations and endothelial leakage are classified as dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS), also termed as severe dengue [9-11]. Laboratory investigations play a critical role in definitive diagnosis and proper management of dengue. In endemic regions, positive tourniquet test and leucopenia {White Blood Cells (WBC) ≤5000 cells/mm^3)} can help in making early diagnosis {Positive Predictive Value Value (PPV): 70-80%)}. Mild thrombocytopenia (100,000 to 150,000 cells/mm^3) is common and about half of all DF patients have platelet count below 100,000 cells/mm^3; but severe thrombocytopenia (<50,000 cells/mm^3) is rare. Haematocrit rise (≈10%) may be found as a consequence of plasma leakage. Serum biochemistry is usually normal but liver enzymes {AST (Aspartate aminotransferase), ALT (Alanine Transaminase)} may be elevated [7].

As the management of dengue fever is mainly supportive, early diagnosis helps in the prevention of various complications. Early diagnosis is possible by a combination of clinical features and haematological parameters, as well as, serology. The gold standard is detection of viruses by viral nucleic acid, antibodies or antigen or a combination of these [10].

During the 2021 dengue epidemic, Uttar Pradesh witnessed one of the biggest outbreaks with a 10-fold increase in the number of reported cases (over 20,000), since 2020 [12]. With each epidemic, it has been observed the clinicohaematological profile and demographics have been changing. With a shift in target population to paediatric age groups, children under the age of 15 years are most susceptible to developing DHF [4]. The purpose of the current study was to identify these changes in clinical presentations, laboratory manifestations and complications for early diagnosis and better management of dengue fever in paediatric patients admitted in a tertiary care hospital, Agra, India.

MATERIALS AND METHODS

The present observational, cross-sectional study was done on patients diagnosed with dengue fever admitted in Department of Paediatrics, FH Medical College, Agra, Uttar Pradesh, India between August 2021 to November 2021. Ethical approval was obtained from Institutional Ethical Committee (FHMC/IEC/R.Cell/2022/18) and informed consent was obtained from all the subjects.

Inclusion criteria: All confirmed dengue cases between one to 18 years of age admitted at FH Medical College, Agra, India confirmed based on the presence of NS1 antigen and/or IgM antibody demonstration serological test by rapid Immunochromatographic Test (ICT) and Enzyme-linked Immunosorbent Assay (ELISA) test were included in the study.

Exclusion criteria: Coinfections with other confirmed cases of enteric fever, malaria, typhus, chikungunya, etc., patients not willing to participate in the study were excluded fron the study.

Study Procedure

All confirmed dengue cases were classified as per WHO guidelines 2009 into three groups [7].

- Dengue
- Dengue with warning sign
- Severe dengue

Data collected from the patients included demographic data, clinical profile of dengue patients, complications and outcomes. Clinical examination included haemodynamic parameters, general and systemic examinations. Haemoglobin, leucocyte count, platelets, haematocrit and other relevant investigations were carried out daily until discharge. Clinical fluid accumulation was considered when pleural effusion or ascites was detected on chest radiography or ultrasonography. Various criterias were used to define laboratory parameters and clinical features [Table/Fig-1] [8,13-15].

Parameters		Reference value
Haemoconcentration		More than 20% increase in haematocrit from baseline.
Leucocytosis		Peripheral WBC more than as per age.
Leukopenia		As a peripheral WBC of less than 5000/µL.
Elevated liver enzymes		Serum ALT and/or AST levels more than 1000 (reference value, 40 U/L).
Ascites	Mild	Diagnosed by ultrasound
	Moderate	On clinical examination shifting dullness present
	Severe	On clinical examination fluid thrill present

[Table/Fig-1]: Criteria used to define laboratory parameters and clinical feature [8,13-15].
WBC: White blood cells; ALT: Alanine transaminase; AST: Aspartate aminotransferase

STATISTICAL ANALYSIS

The data was collected in Microsoft Excel sheet, analysed and represented in the form of numbers and percentages.

RESULTS

In the present study, a total of 801 dengue patients were included as per the inclusion criteria. Among them, 486 (60.67%) were males and 315 (39.33%) were females. Most cases were in between the age group 10-18 years (38.45%) followed by the age group 5-10 years (34.83%). Only 56.55% cases were from urban areas, while 43.44% cases were from rural area [Table/Fig-2].

Demographic profile of patients	
Characteristics	**n (%)**
Age	
1 month to 1 year	52 (6.49)
2-5 years	162 (20.22)
6-10 years	279 (34.83)
11-18 years	308 (38.45)
Gender	
Male	486 (60.67)
Female	315 (39.32)
Location	
Rural	348 (43.44)
Urban	453 (56.55)

[Table/Fig-2]: Demographic profile of dengue (N=801).

Distribution: According to WHO classification, most cases (49.82%) were dengue with warning signs followed by 28.3% cases of severe dengue and 21.84% cases of dengue without warning signs [Table/Fig-3].

Classification	n (%)
Dengue with warning signs	399 (49.82)
Dengue without warning signs	175 (21.84)
Severe dengue	227 (28.34)
Total	801(100)

[Table/Fig-3]: Dengue cases classification.

Clinical features: The commonest symptom was fever (97.25%) followed by body pain/arthralgia (87.39%), flushing (77.65%), abdominal pain (54.55%) and vomiting (53.43%). Bleeding (nasal bleeding, gastrointestinal bleeding, and intracranial bleeding) was present in 45.69% cases and 15.60% cases had hypotension. 46.81% cases had hepatomegaly and 47.19% cases had splenomegaly. A total of 31.21% cases had cough, while 12.48% cases had respiratory failure due to pleural effusion or pulmonary oedema. A total of 18.15% cases had altered sensorium and 6.74% cases had seizures, which might have been due to dengue encephalitis or intracranial bleeding [Table/Fig-4].

Clinical features of dengue	
Symptoms	**n (%)**
Fever	779 (97.25)
Body pain/Arthralgia	700 (87.39)
Flushing	622 (77.65)
Itching	520 (64.91)
Abdominal pain	437 (54.55)
Vomiting	428 (53.43)
Skin erythema	400 (49.93)

Splenomegaly	378 (47.19)
Hepatomegaly	375 (46.81)
Bleeding	366 (45.69)
Anorexia	339 (42.32)
Petechial	325 (40.57)
Retro-orbital pain	257 (32.08)
Cough	250 (31.21)
Headache/Myalgia	234 (29.21)
Oedema	221 (27.59)
Loose stools	160 (19.97)
Altered sensorium	147 (18.35)
Nasal discharge	128 (15.98)
Hypotension	125 (15.60)
Jaundice	123 (15.35)
Respiratory failure	100 (12.48)
Sore throat	75 (9.36)
Seizures	72 (9)
Lymphadenopathy	43 (5.36)

[Table/Fig-4]: Clinical features of dengue (N=801).

Haematological features: A total of 78.15% cases were NS1 antigen positive, 41.44% were IgM positive. Laboratory findings reveal that leucopenia was seen in 22.09% patients, whereas 25.46% patients had leucocytosis. A total of 94.75% cases had thrombocytopenia. The lowest platelet count noted in the present study was 4000/ mm^3. Haematocrit was increased in 39.45% cases. AST and ALT were raised in 44.81% and 46.24% cases, respectively [Table/Fig-5].

Variables	n (%)
Chest X-ray (Total number of chest X-rays=250)	
Normal	107 (42.8)
Unilateral	32 (12.8)
Bilateral	35 (14)
Pleural effusion	67 (26.8)
Abdominal USG (Total number of USG=101)	
Normal	82 (81.18)
Ascites present	12 (11.88)
Mild	7 (6.93)
Moderate	3 (2.97)
Severe	2 (1.98)
Acalculous cholecystitis	7 (6.93)
CT/MRI brain (Total number of neuroimaging=21)	
Normal	11 (52.38)
Infarction	7 (33.33)
Cerebral oedema	3 (1.69)
Haematological parameters (Total number of haemograms=801)	
Increased haematocrit	316 (39.45)
Leucopenia	177 (22.09)
Leucocytosis	204 (25.46)
Thrombocytopenia	759 (94.75)
Abnormal PT/INR	197 (24.59)
Increased AST	359 (44.81)
Increased ALT	351 (46.24)
NS1 antigen	626 (78.15)
IgG	268 (35.7)
IgM	332 (41.44)

[Table/Fig-5]: Laboratory investigation and imaging studies in dengue. USG: Ultrasonography; CT: Computed tomography; PT: Prothrombin time; INR: International normalised ratio; AST: Aspartate aminotransferase; ALT: Alanine transaminase; Ig: Immunoglobulin

Radiological features: Chest X-ray was done in 250 cases, out of these 14% had bilateral pleural effusion and 12.8% had unilateral pleural effusion. USG abdomen was done in 101 cases, out of these 11.88% had ascites and 6.93% had acalculous cholecystitis. Neuroimaging was done in 21 cases, out of these 33.33% had infraction and 1.69% had cerebral oedema [Table/Fig-5].

Mortality: Out of 801 patients admitted, 76.27% were cured, 10.11% expired and 13.6% went on leave against medical advice [Table/Fig-6].

Outcome	n (%)
Cured	611 (76.27)
Expired	81 (10.11)
Leave Against Medical Advice (LAMA)	109 (13.6)
Total	801 (100)

[Table/Fig-6]: Patient outcome during dengue.

DISCUSSION

A vast majority of dengue cases are asymptomatic or mild and self-managed, and hence, the actual numbers of dengue cases are under-reported. Many cases are also misdiagnosed as other febrile illnesses [16]. In the present study, a wide range of manifestations were observed with approximately 27% of patients diagnosed as severe dengue and a number of these patients had atypical manifestations. Most of the patients affected were males between the ages of 10 to 18 years, which was similar to other studies carried out in India. This may have been due to more exposure of male children in outdoor activities during the day timings [17]. In present study, most organ systems were affected by dengue virus, from cutaneous manifestations to neurological illnesses.

The clinical manifestations of dengue fever are quite variable depending upon the age of the patient and the type of infecting strain of virus [18]. Fever was the most common symptom, present across the spectrum of non severe and severe dengue in 97% of the patients admitted. This finding is correlated by all studies on dengue [6,9,10]. Dengue cutaneous manifestations range from maculopapular rash to petechial and flushing. In the present study, the prevalence of rash and flushing were 49.93% and 77.65%, respectively. This was comparatively similar to data reported by Sud R and Nair V, and Majeed IA et al., (10% and 44% of maculopapular and flushing, respectively) [6,10]. In the present study, large (64.91%) number of patients developed complaints of itching, which was significantly higher (28.6%) than that found in a meta-analysis by Nguyen DK et al., [19]. Itching is caused by inflammatory cell infiltration and dermal oedema due to increased vessel permeability; cytokines released from the damaged blood vessels during the host and virus interaction, and suggestive of a vigorous immune response [20].

Pleural effusion and ascites are the complications of dengue fever resulting from the plasma leakage into the pleural cavity [21]. The present study showed pleural effusion in 26.8% cases, and ascites in 11.88%. Shabbir M et al., found 12.6% cases of pleural effusion as opposed to Kumar A et al., who found pleural effusion in 20% cases [22,23]. Rahman MA et al., found a 34% prevalence of ascites in their study [9].

Patients also presented with neurological manifestations like headache, altered sensorium and seizures in the present study. Headache occurred due to inflammatory markers and is a commonly reported symptom. In the present study, headache was present in 29.21% of children, while Laul A et al., and Avasthi S et al., reported headache in 87% and 9% respectively [24,25]. After headaches, altered sensorium (18.35%) was the next most common Central Nervous System (CNS) manifestation followed by seizures (9%). Mehta VK et al., found altered sensorium in 90% and seizures in 51% of their dengue encephalitis cases [26].

Abdominal pain and vomiting are cardinal in dengue. The present study showed a prevalence of abdominal pain and vomiting 54.55% and 53.43% respectively, which were higher in comparison to Majeed IA et al., (24.61% and 39.23%, respectively and Dhobale RV et al., (43% and 37%, respectively) [10,17]. It is due to more hepatic involvement by dengue virus in the paediatric age group. On examination, 46.81% and 47.91% of patients had hepatomegaly and splenomegaly respectively. Studies by Majeed IA et al., also showed 46.15% and 11.53% prevalence of hepatomegaly and splenomegaly respectively however Dhobale RV et al., only found an 11% prevalence of hepatomegaly [10,17]. Collaborating with the complaint of abdominal pain and finding of hepatosplenomegaly (with or without tenderness), hepatic transaminase levels were monitored. In the present study, 44.81% and 46.24% cases showed elevated AST and ALT levels, respectively. Study by Prasanna N et al., also reported a statistically significant number (ALT in 31% and AST in 22%) of patients who had elevated transaminases [27].

All patients were confirmed with serodiagnosis. In the absence of Polymerase Chani Reaction (PCR) viral detection, serodiagnosis tools are an effective and economical means to establish a diagnosis. In the present study NS1Ag, Dengue IgM and Dengue IgG were positive in 78.15%, 35.7% and 41.44% cases, respectively. The NS1Ag test has a sensitivity of 77.3% (15 mins), 80.5% (30 mins) and specificity of 100% (15 and 30 mins post testing) [28]. The presence of IgG in 41.44% of patients indicated previous dengue infection which contributed to the large numbers of DSS/DHF patients. Study of Dhobale RV et al., showed antigen positivity rates of 20, 31, 23% of NS1Ag, Dengue IgM, IgG, respectively [17].

Thrombocytopenia and leucopenia are common findings in dengue fever, especially lymphopenia is found near the end of the febrile phase. A platelet count of 100,000/mm^3 is usually found between day 3 and day 8 of illness. Cytopenias are believed to be caused by direct destructive actions of the virus on bone marrow precursor cells. The resulting active viral replication and cellular destruction in the bone marrow, are believed to cause the bone pain [20].

In the present study, thrombocytopenia was seen in 94.75% cases and leucopenia in 22.09% cases. Kulkarni RD et al., showed thrombocytopenia in 68.75% patients [29]. Thrombocytopenia may lead to bleeding. A total of 45.69% (366) patients had bleeding manifestations in the form of: gum bleed, epistaxis, haematemesis and melena. Study by Avasthi S et al., demonstrated 8% patients had bleeding episodes, while 26% patients had platelet count below 20,000/mm^3 and 84% had platelet <100,000/mm^3 [25]. While according to Laul A et al., haemorrhagic manifestations: hematemesis, melena and epistaxis were found in 21% however, only 12.85% cases had platelet count <70,000/mm^3 [24]. In study by Khan AH et al., only 5% patients had bleeding, while 40% had thrombocytopenia [30]. These findings show thrombocytopenia is very common in dengue, but not every child with thrombocytopenia has bleeding manifestation.

To maintain body haemostasis, clotting factors and platelets are required. In the present study, the Prothrombin Time (PT)/ International Normalised Ratio (INR) of 636 patients was done with 24.6% having deranged PT/INR warranting administration of vitamin K injection and/or transfusion of fresh frozen plasma. Adane T and Getawa S, meta-analysis reported PT/INR derangement in 13.4% of paediatric cases [31]. Higher incidence of coagulopathy in present study, might be due to more cases of reinfection.

A key parameter to watch in haemogram of dengue patients is raised haematocrit, as it suggests increased risk of third space loss of intravascular fluid in effect increasing the viscosity of the blood, causing stasis. Thus, requiring judicious fluid management with intravenous fluid therapy. In the present study, 39.45% cases had raised haematocrit which is comparable to 36%, reported by Prasanna N et al., [27]. The present study also showed leucopenia in 22.9% patients, as compared to 31% seen in the study by Prasanna N et al., [27]. The present study had a mortality of 10%, which is comparable to 13.75%, reported by Prasad D and Bhriguvanshi A [32]. This is largely attributed to many patients presenting to the hospital, in the later stages of the DSS/DHF with atypical manifestations like dengue encephalitis. Due to the outbreak, sample size was large enough to represent the paediatric population. The present study presents the latest trends in clinical and laboratory parameters of dengue in the paediatric age group.

Limitation(s)

The limitation of the present study was that, virus serotyping investigation was not done.

CONCLUSION(S)

Dengue is a very dreadful vector-borne disease, especially in the paediatric population. Despite various national and state level control programmes, complications and severity of dengue fever is increasing with each outbreak. Complications like pleural effusion, ascites and bleeding manifestation were quite common in the present study. Atypical presentations like CNS involvement and hepatic involvement were high, as compared to previous studies. Early diagnosis on the basis of high clinical suspicion and haematological parameters and early fluid management, can save many lives.

REFERENCES

[1] Simmons CP, Farrar JJ, Nguyen van VC, Wills B. Dengue. N Engl J Med. 2012;366(15):1423-32. Available from: http://dx.doi.org/10.1056/NEJMra1110265.

[2] Lambrechts L, Scott TW, Gubler DJ. Consequences of the expanding global distribution of Aedes albopictus for dengue virus transmission. PLoS Negl Trop Dis. 2010;4(5):e646. Available from: http://dx.doi.org/10.1371/journal.pntd.0000646.

[3] Stanaway JD, Shepard DS, Undurraga EA, Halasa YA, Coffeng LE, Brady OJ, et al. The global burden of dengue: An analysis from the global burden of disease study 2013. Lancet Infect Dis. 2016;16:712-23. https://doi.org/10.1016/S1473-3099(16)00026-8.

[4] Geneva: World Health Organisation; 2022. DENGUE AND SEVERE DENGUE. 2022 Geneva. Updated 10 Jan 2022; Accessed 11 December 2021]. Available at: <https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>.

[5] Geneva: World Health Organisation; 2022. World Population Prospects. Summary of results. 2022. Geneva. Available from: https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/wpp2022_summary_of_results.pdf. [Accessed Sept 20 2022].

[6] Sud R, Nair V. Is the clinicopathological profile of dengue syndrome changing? A 6 year study of different epidemics at a tertiary care center in India. International Journal of Advances in Medicine. 2020;7(3):457-46. Doi: 10.18203/2349-3933.ijam20200658.

[7] Geneva: World Health Organisation; 2009. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control: Geneva; 2009. Available from: https://apps.who.int/iris/handle/10665/44188. [Accessed Sept 20 2022].

[8] Kyle JL, Harris E. Global spread and persistence of dengue. Annu Rev Microbiol. 2008;62:71-92. Doi: 10.1146/annurev.micro.62.081307.163005. PMID: 18429680.

[9] Rahman MA, Begum MUH, Uddin HMN, Monica S, Millat MB. Clinicopathological profile and outcome of dengue fever: A tertiary Can hospital experience. J Bangladesh Coll Pays Surg. 2021;39:213-19. http://doi.org/10.3329/jbcps.v39i4.55941.

[10] Majeed IA, Avabratha KS, Gowda LR, Syeda S. Clinicohaematological profile of dengue in children: A hospital based study. Int J Contemp Pediatr. 2017;4(4):1340-44. Doi: http://dx.doi.org/10.18203/2349-3291.ijcp20172662.

[11] Statler J, Mammen M, Lyons A, Sun W. Sonographic findings of healthy volunteers infected with dengue fever. J Clin Ultrasound. 2008.36(7):413-17. http://doi.org/10.1002/jcu.20476. PMID: 003A18446859.

[12] National Center for Vector Borne Diseases Control. India. Directorate General of Health Services, Ministry of health and family welfare. 2022 Dengue/DHF Situation In India: Dengue Cases and Deaths in the Country since 2015. [Updated: September 13, 2022; cited 9 December 2021]. Available from: <https://nvbdcp.gov.in/index4.php?lang=1&level=0&linkid=431&lid=3715>.

[13] Padmaprakash KV, Jha VK, Bhushan S, Deepkamal, Sowmya KC. Demographic and clinical profile of dengue fever in a tertiary care hospital of South India. J Assoc Physicians India. 2020;68(11):24-27. PMID: 33187032.

[14] Stanley F. Lo. Reference Interval for Laboratory test and procedures Kliegman, Robert. Nelson Textbook of Paediatrics First south Asia Ed. New Delhi, PA: Elsevier. 2016;3464-66.

[15] Bavdekar A, Thakur N. Ascites in children. Indian J Pediatr. 2016;83(11):1334-40. Doi: 10.1007/a12098-016-2168-1. Epub 2016 Jun 9. PIMD:27278239.

[16] Waggoner JJ, Gresh L, Vargas MJ, Ballesteros G, Tellez Y, Soda KJ, et al. Viremia and clinical presentation in Nicaraguan patients infected with zika virus, chikungunya virus, and dengue virus. Clin Infect Dis. 2016;63(12):1584-90. Doi: 10.1093/cid/ciw589. PMID: 27578819; PMCID: PMC5146717.

[17] Dhobale RV, Gore AD, Waghachavare VB, Kumbhar SG, Kadam YR, Dhumale GB, et al. Clinical and laboratory characteristics of pediatric dengue fever patients in a tertiary care hospital. Natl J Community Med. 2015;7(01):21-24. Available from: https://www.njcmindia.com/index.php/file/article/view/846.

[18] Thach TQ, Eisa HG, Hmeda AB, Faraj H, Thuan TM, Abdelrahman MM, et al. Predictive markers for the early prognosis of dengue severity: A systematic review and meta-analysis. PLoS Negl Trop Dis. 2021;15(10):01-25. Available from: http://dx.doi.org/10.1371/journal.pntd.0009808.

[19] Nguyen DK, El-Qushayri AE, Ahmed AM, Safi A, Mageed SA, Mehyar SM, et al. Association of allergic symptoms with dengue infection and severity: A systematic review and meta-analysis. Virol Sin. 2020;35(1):83-92. Doi: 10.1007/s12250-019-00165-6. PMID: 31637633 PMCID: PMC7035405.

[20] Huang HW, Tseng HC, Lee CH, Chuang HY, Lin SH. Clinical significance of skin rash in dengue fever: A focus on discomfort, complications, and disease outcome. Asian Pac J Trop Med. 2016;9(7):713-18. Doi: 10.1016/j.apjtm.2016.05.013 PMID: 27393104.

[21] Smith D, Mariano D, ML Trautwein. 2022. Dengue: Practice Essentials, Background, Pathophysiology. [online] Emedicine.medscape.com. Available at: <https://emedicine.medscape.com/article/215840-overview> [Accessed 17 January 2022].

[22] Shabbir M, Ameen F, Roshan N, Israr M. Nature and clinical course of pleural effusion in dengue fever. Int J Intern Emerg Med. 2018;1(1):1006.

[23] Kumar A, Rao C, Pandit V, Shetty S, Bammigatti C, Samarasinghe C, et al. Clinical manifestations and trend of dengue cases admitted in a tertiary care hospital, Udupi district, Karnataka. Indian J Community Med. 2010;35(3):386-90. Doi: 10.4103/0970-0218.69253.

[24] Laul A, Laul P, Merugumala V, Pathak R, Miglani U, Saxena P, et al. Clinical profiles of dengue infection during an outbreak in northern India. J Trop Med. 2016:01-07. Doi: 10.1155/2016/5917934.

[25] Avasthi S, Singh VK, Kumar S, Kumar A, Dutta S. The changing spectrum of dengue fever in the 2009 epidemic in North India: A tertiary teaching hospital based study. J Clin Diagn Res. 2012;6(6):999002.

[26] Mehta VK, Verma R, Jain A, Sharma N, Mahdi AA. A study of dengue encephalitis with laboratory and clinical parameters in Tertiary Center of North India, Journal of Family Medicine and Primary Care. 2021;10(11):4041-46. Doi: 10.4103/jfmpc.jfmpc_632_21.

[27] Prasanna N, Punyashetty KB, Ananthrao AS, Patil T. Clinico-hematological profile in dengue: A tertiary care institutional study. Indian Journal of Pathology: Research and Practice. 2017;6(1):75-81. Doi: http://dx.doi.org/10.21088/ijprp.2278.148X.6117.12.

[28] Chaterji S, Allen JC, Jr Chow A, Leo YS, Ooi EE. Evaluation of the NS1 rapid test and the WHO dengue classification schemes for use as bedside diagnosis of acute dengue fever in adults. Am J Trop Med Hyg. 2011;84(2):224-28. https://doi.org/10.4269/ajtmh.2011.10-0316.

[29] Kulkarni RD, Patil SS, Ajantha GS, Upadhya AK, Kalabhavi AS, Shubhada RM, et al. Association of platelet count and serological markers of dengue infection- importance of NS1 antigen. Indian J Med Microbiol. 2011;29(4):359-62. Doi: 10.4103/0255-0857.90159. PMID: 22120794.

[30] Khan A, Hayat A, Masood N, Solangi N, Shaikh T. Frequency and clinical presentation of dengue fever at tertiary care hospital of Hyderabad/Jamshoro. Journal of Liaquat University of Medical and Health Sciences. 2010;09(02):88-94. Available from: https://www.lumhs.edu.pk/jlumhs/Vol09No02/pdfs/v9n2oa08.pdf.

[31] Adane T, Getawa S. Coagulation abnormalities in dengue fever infection: A systematic review and meta-analysis. PLoS Negl Trop Dis. 2021;15(8):01-16. Doi: 10.1371/journal.pntd.0009666. PMID: 34407078; PMCID: PMC8372965.

[32] Prasad D, Bhriguvanshi A. Clinical Profile, Liver Dysfunction and Outcome of Dengue Infection in Children: A Prospective Observational Study. Pediatr Infect Dis J. 2020;39(2):97-101. doi: 10.1097/INF.0000000000002519. PMID: 31815826.

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Paediatrics, FH Medical College, Agra, Uttar Pradesh, India.
2. Associate Professor, Department of Paediatrics, FH Medical College, Agra, Uttar Pradesh, India.
3. Junior Resident, Department of Paediatrics, FH Medical College, Agra, Uttar Pradesh, India.
4. Junior Resident, Department of Paediatrics, FH Medical College, Agra, Uttar Pradesh, India.
5. Professor and Head, Department of Paediatrics, FH Medical College, Agra, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Shehraz Firoz,
Associate Professor, Department of Paediatrics, FH Medical College,
Agra, Uttar Pradesh, India.
E-mail: dr.shehrazfiroz@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: Jul 28, 2022
- Manual Googling: Sep 22, 2022
- iThenticate Software: Sep 26, 2022 (14%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jul 21, 2022**
Date of Peer Review: **Aug 31, 2022**
Date of Acceptance: **Sep 27, 2022**
Date of Publishing: **Dec 31, 2022**