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Serological insights and clinical patterns of dengue fever in a tertiary care hospital: a survey-based study

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Abstract

Background: Dengue fever, a vector-borne disease caused by the dengue virus (DENV) and transmitted by Aedes mosquitoes, remains a public health concern in India, especially due to its seasonal and geographical variability. The disease manifests with symptoms like fever, myalgia, rashes, leukopenia, and thrombocytopenia, affecting various organs. This study aimed to examine the demographic patterns, clinical presentations, and healthcare-seeking behavior of paediatric dengue patients. Additionally, it analyzed dengue positivity trends from 2021 to 2023.

Methods: A descriptive cross-sectional study was conducted from September to December 2021 among suspected dengue paediatric patients admitted to the Paediatrics department of Autonomous State Medical College Firozabad. Diagnostic tests included Dengue rapid NS1, ELISA NS1 Antigen, and IgM ELISA. Data were analyzed to assess clinical symptoms, healthcare access, and yearly dengue trends.

Results: A total of 6,445 patients were clinically suspected of dengue at the Paediatrics IPD, Autonomous State Medical College, Firozabad, Uttar Pradesh. Among them, 386 were confirmed dengue-positive by rapid card, NS1 antigen, or IgM ELISA tests. The highest number of suspected cases (43.17%) was observed in school-going children (6–12 years). Males (55.47%) were more affected than females (44.53%), with nearly equal distribution between rural and urban areas. Platelet counts varied widely, with 31.73% having counts between 50,000–100,000. Fever with myalgia (75.65%) was the most common symptom. Dengue positivity fluctuated across years, with the highest rate in 2021 (193/1147 cases), followed by declines in 2022 and 2023.

Conclusion: Dengue fever shows a variable trend in incidence, with significant impact from healthcare access and public awareness. Improving awareness and timely diagnosis could help mitigate the severity of cases in future outbreaks.

Keywords: Dengue, Paediatric Case, ELISA, Clinical Manifestation, Positivity Trends, India

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Background

Dengue fever, a vector-borne viral disease caused by the dengue virus (DENV) and transmitted primarily by Aedes mosquitoes, presents a significant public health challenge in India. It is a benign syndrome manifested by biphasic fever, myalgia or arthralgia, rashes, leukopenia, and lymphadenopathy. The manifestation of this fever varies with age and from patient to patient. It also varies in severity and ranges from mild symptoms to life-threatening conditions [1]. Three key factors drive the increase in dengue outbreaks: the continued expansion of urbanization in tropical regions, particularly in Asia; the failure of mosquito control measures in these urban areas, which creates favorable conditions for disease transmission; and the rise in global air travel, which accelerates the spread of dengue viruses within the population [2]. This arthropod-borne arboviral disease and is mostly transmitted in humans through mosquitoes, particularly those in the Aedes genus, among which Aedes aegypti are the principal and aggressive day biters. These vectors are highly urbanized and breed in artificially stored water. The virus (DENV) belongs to the Flaviviridae family and has four serotypes including DENV-1, DENV-2, DENV-3, and DENV-4 and all serotypes cause human infection [3]. According to a study, Dengue virus serotype-2 (DENV 2) emerged as the most prevalent serotype, constituting 34% of cases, and exhibited the highest percentage of severe dengue incidents at 20.6% [4].

Dengue fever presents a range of symptoms depending on the severity. Uncomplicated cases are manifested by high-grade biphasic fever, severe headache, joint and muscle pain, pain behind the eyes, fatigue, nausea, and vomiting. On the other hand, complicated cases present warning signs such as rashes, easy bleeding and bruising, severe abdominal pain, persistent vomiting, blood in stool or urine, hypotension, and other features of shock. In accordance with the WHO's 1997 classification of dengue, cases were categorized into three groups: dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS). Furthermore, as many cases presented with symptoms falling between these classifications, the criteria were revised in 2009, effectively creating categories of severe dengue and non-severe dengue cases [5]. India, with its tropical climate and monsoon patterns, provides an optimal environment for Aedes mosquitoes, particularly Aedes aegypti and Aedes albopictus. The incidence of dengue fever in India exhibits seasonal and geographical variability, with peak transmission occurring during and immediately after the monsoon season. Aedes mosquitoes, predominantly breeds in artificial water reservoirs such as buckets and discarded tires, lay eggs singly just above the waterline. Climate factors, especially temperature and rainfall, significantly influence their lifecycle, breeding, and lifespan, impacting disease transmission. Ae. aegypti usually survives approximately 30 days. During rainy seasons when survival is extended, the risk of virus transmission rises [6]. Female Aedes aegypti mosquito biting frequencies are impacted by temperature, with the potential risk rising to about 31-47% due to a temperature increase of approximately 10°C [7]. This research was conducted to gain a deeper understanding of the demographic distribution patterns of dengue fever and its diverse clinical manifestations. Additionally, it aimed to explore how access to healthcare, risk perception, and availability of information on dengue symptoms impact individuals' decisions to seek medical help. This comprehensive analysis is vital for improving public health strategies, enhancing early detection, and effectively managing dengue outbreaks. This study aims to analyze the magnitude of dengue waves in 2021, 2022, and 2023, assess the severity of the 2021 outbreak by demographic factors, and evaluate the correlation between platelet count decline and disease severity.

Methods Study design

A descriptive cross-sectional study was conducted to analyze the clinical features, serological patterns, and demographic distribution of dengue fever cases admitted in the Pediatrics Department of Autonomous State Medical College, Firozabad, Uttar Pradesh. The study spanned September to December 2021, covering the post-monsoon season, a period recognized for increased dengue transmission. The study was designed to understand the magnitude and impact of dengue fever during the reported outbreak.

Study Population and Sampling

The study included 6,445 clinically suspected cases of dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) among pediatric patients admitted to the inpatient department. Patients were selected based on the specific inclusion criteria defined by the World Health Organization

(WHO) guidelines for dengue diagnosis. Cases ranged across various age groups, from neonates to adolescents, and were further categorized into six demographic groups: newborns, infants, toddlers, preschoolers, school-age children, and adolescents. Written informed consent was obtained from the parents or legal guardians of the participants before their inclusion in the study.

Procedure of Data Collection

Data collection involved a thorough review of indoor patient files, capturing clinical, demographic, and laboratory details. The following data sources were utilized:

- **1. Admission records:** Demographic details (age, sex, and residential area) and duration of hospital stay.
- **2. Physical examination findings:** Documented by the attending physicians.
- **3. Laboratory reports:** Results from hematological investigations, including platelet counts, and results of dengue serological tests (NS1 Antigen, IgM ELISA, and Dengue Rapid Card).
- **4. Follow-up records:** Daily observations of clinical symptoms, platelet counts, transfusion requirements, and treatment outcomes.

Diagnostic Criteria

The study relied on the following diagnostic methods for confirming dengue infection:

- 1. NS1 Antigen Test.
- 2. Dengue Rapid Card Test.
- 3. IgM ELISA Test.

Patients testing positive for any of these diagnostic methods were classified as confirmed dengue cases. The study further stratified patients based on their clinical manifestations (fever with myalgia, gastrointestinal symptoms, respiratory symptoms, etc.) and their platelet count ranges (<10,000 to >150,000).

Study Parameters

The study focused on the following parameters:

- 1. Magnitude of suspected dengue cases: Distribution across age, sex, and residential areas.
- **2. Endemicity severity:** Analysis of the 2021 outbreak, including hospitalization patterns and platelet levels.
- **3. Correlation between platelet count and clinical severity:** Exploration of how thrombocytopenia related to specific clinical symptoms such as fever with myalgia, gastrointestinal manifestations, and respiratory symptoms. The findings highlighted the predominance of school-going children (6–12 years) among suspected cases and a slight male predominance (55.47%). Rural and urban populations were almost equally represented. Platelet counts <100,000 were prevalent in 60% of cases, and fever with myalgia emerged as the most common symptom in 75.65% of cases. Serological testing over three years (2021–2023) showed fluctuating trends in positivity rates, with the highest rates recorded in 2021.

Statistical analysis

Data from the patient records were systematically entered into an MS Excel spreadsheet and subsequently analyzed using Epi Info Software Version 7.2.5.0. Descriptive statistics, including frequencies and percentages, were used to describe the clinical

and demographic characteristics of the study population. Trends in serological positivity and the correlation between platelet counts and clinical manifestations were analyzed. The data also allowed a year-wise comparison of the magnitude and serological testing outcomes for 2021, 2022, and 2023.

Results

Total 6445 patients visited in the IPD of Department of Paediatrics at Autonomous State Medical College, Firozabad Uttar Pradesh were suspected for Dengue during September to December 2021. Among the 6445 clinically suspected cases admitted in the paediatric ward, 386 were found to be Dengue positive by any of the three criteria i.e. Dengue rapid card, NS1 antigen, or Ig M ELISA test. As figure 1 shows out of those 6445 clinically suspected patients 02(0.03%) were new-born, 710(11.02%) patients were infant, 720(11.17%) patients were toddlers, 1181(18.32%) patients were pre-school group, 2782(43.17%) patients were from school going group and 1050(16.29%) patients were among the adolescent age group. Among all these the most dominant group was school going age group (age-6 to 12 years) with the higher numbers of clinically suspected dengue cases 2782(43.17%) of all the patients. As figure-2 shows, there were 2870(44.53%) female and 3575 (55.47%) males as well as there were 3202(49.68%) from rural area and 3243(50.32%) from urban area as figure 3 shows.

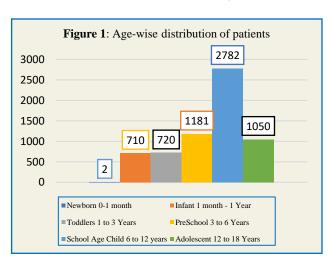


Figure 1: Age-wise distribution of patients admitted in Dengue ward (2021)

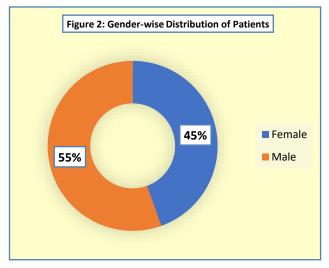


Figure 2: Gender-wise distribution of patients admitted in Dengue ward (2021)

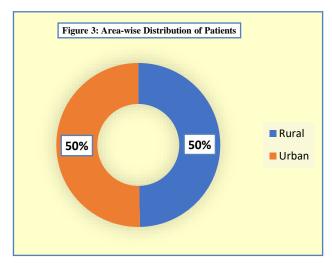


Figure 3: Resident area distribution of patients admitted in Dengue ward (2021)

Clinical Profile of Patients

As figure 4 depicts, among 6445 suspected cases of Dengue, the patients having platelet count less than 10,000 were 58(0.90%), between 10 to 20k were 488(7.57%), between 20 to 50k were 1295(20.09%), between 50 to 100k were 2045(31.73%), between 100 to 150k were 1353(20.99%) and with more than 150k platelet count were 1206(18.71%).

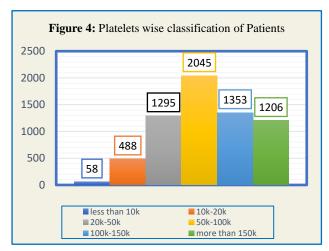


Figure 4: platelets-wise classification of patients admitted in Dengue ward (2021)

Table 1 depicts that among patients suspected of having dengue fever, the most prevalent symptom presentation is fever accompanied by myalgia in 3255(75.65%) cases. This myalgia is frequently reported as generalized body aches or joint pain, reflecting the systemic nature of the disease. The next most common symptom presentation involves fever associated with gastrointestinal symptoms, such as diarrhoea and vomiting, which are indicative of the disease's impact on the digestive system in 869(20.17%) cases. Following these, the occurrence of fever with respiratory symptoms in 81(1.88%) cases, though less common, was also noted. This pattern of symptoms highlights the multi-system involvement in dengue fever, with musculoskeletal and gastrointestinal manifestations being particularly prominent. This table provides insight into the relationship between platelet counts and various clinical symptoms, helping to understand how platelet levels might correlate with the presentation and severity of symptoms in patients. The majority of patients exhibiting predominant GI symptoms and Myalgia had platelet counts in the range of 50,000 to 100,000. This was followed by patients with Myalgia,

Respiratory symptoms, and GI symptoms who had platelet counts exceeding 150,000. Patients with critical platelet counts displayed less diversity in symptoms than anticipated.

Table 1: Clinical Manifestations of dengue Patients

Platelet Count	Fever with	Fever	Fever	Fever	Fever with	Fever	Fever	Fever with	Total
	GI and	With GI	with	with	Respiratory	with	with	Swelling of	
	Respiratory	symptoms	Hypotension	Myalgia	Symptoms	Shock	Anaemia	body	
	Symptoms								
less than 10k	0	2	0	7	0	0	0	0	9
10k-20k	0	25	0	70	4	1	1	0	101
20k-50k	3	185	1	618	4	15	2	1	829
50k-100k	5	346	2	1141	7	21	1	1	1524
100k-150k	2	120	1	517	7	6	1	0	654
more than 150k	9	191	0	902	59	25	3	0	1189
Total	19	869	4	3255	81	68	8	2	4306

Table 2 details the positive Dengue Rapid NS1 test results by clinical manifestation: Fever with Myalgia had the highest number of positive cases, totaling 315. There was 1 positive case each for Fever with GI and Respiratory Symptoms and Fever with Anaemia.

Fever with GI Symptoms had 64 positive cases, Fever with Hypotension had 2, Fever with Respiratory Symptoms had 3, and Fever with Shock had 1 positive case. No positive cases were recorded for Fever with Skin Rashes or Fever with Swelling of Body.

Table 2: Clinical Manifestation of fever In Dengue patients based on Dengue Rapid NS1 Antigen Test Results

Dengue Rapid NS1 (Clinical Manifestations)	Negative	Positive	Total
Fever with Myalgia	613	315	928
Fever with GI and Respiratory Symptoms	0	1	1
Fever with GI symptoms	125	64	189
Fever with Hypotension	2	2	4
Fever with Respiratory Symptoms	13	3	16
Fever with Shock	7	1	8
Fever with Skin Rashes	0	0	0
Fever, Anaemia	1	0	1
Fever, Swelling of the body	0	0	0
Grand Total	761	386	1147

Table 3 shows the distribution of positive Dengue ELISA NS1 test cases: Fever with Myalgia had the highest number, with 251 positive cases. Fever with GI symptoms had 80 positive cases, while Fever with Respiratory Symptoms had 9 positive cases.

Fever with Shock had 6 positive cases, and Fever with GI and Respiratory Symptoms had 3 positive cases. No positive cases were recorded for Fever with Hypotension, Fever with Skin Rashes, or Fever with Swelling of Body.

Table 3: Clinical Manifestation of fever In Dengue patients based on Dengue ELISA NS1 Antigen Test Results

Dengue ELISA NS1 (Clinical Manifestations)	Negative	Positive	Total
Fever with GI and Respiratory symptoms	0	3	3
Fever with GI symptoms	30	80	110
Fever with Hypotension	0	0	0
Fever with Myalgia	163	251	414
Fever with Respiratory Symptoms	13	9	22
Fever with Shock	4	6	10
Fever with Skin Rashes	0	0	0
Fever, Anaemia	2	0	2
Fever, Swelling of body	0	0	0
Grand Total	212	349	561

Table 4 shows Dengue ELISA IgM test results by clinical manifestation: Fever with Myalgia has the highest number of positive cases, a total of 144. Fever with GI symptoms was found in 37 positive cases. Fever with Respiratory Symptoms and Fever with Shock each have 6 positive cases.

Fever with GI and Respiratory Symptoms, Fever with Anaemia, and other symptoms such as Fever with Skin Rashes and Fever with Swelling of Body have no positive cases. In total, 193 patients tested positive and 267 tested negatives out of 460 patients.

Table 4: Clinical Manifestation of fever In Dengue patients based on Dengue ELISA IgM Antibody	ody Test Results
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Dengue ELISA IgM (Clinical Manifestations)	Negative	Positive	Total
Fever with GI and Respiratory Symptoms	1	0	1
Fever with GI symptoms	53	37	90
Fever with Hypotension	0	0	0
Fever with Myalgia	190	144	334
Fever with Respiratory Symptoms	15	6	21
Fever with Shock	6	6	12
Fever with Skin Rashes	0	0	0
Fever, Anaemia	2	0	2
Fever, Swelling of the body	0	0	0
Grand Total	267	193	460

Table 5 provides an overview of Dengue ELISA testing outcomes for the years 2021, 2022, and 2023. In 2021, a total of 1,147 tests were performed, yielding 193 positive results, indicating a high positivity rate. In 2022, the number of tests decreased to 862, with a significantly lower number of positive

cases, totaling 30. In 2023, the number of tests increased to 1,231, and the number of positive cases rose to 61. This data reflects a fluctuating trend in Dengue positivity over the three years, with 2021 showing the highest positivity rate, followed by a decrease in 2022 and a partial increase in 2023.

Table 5: Year-wise Dengue patients based on Dengue ELISA IgM Antibody Test

Dengue ELISA				
Year	Total test Conducted	Total Found positive		
2021	1147	193		
2022	862	30		
2023	1231	61		

Discussion

Dengue is emerging as a prevalent health issue in India, with endemic prevalence in certain regions and occasional annual outbreaks during the monsoon season. Annually, each outbreak results in high morbidity and mortality. According to reports of National Centre for Vector Borne Diseases Control, 2022, there were about 2.5 lakhs reported cases of dengue in India and 67, 271 in U.P alone. The impact of each outbreak is most severe in North India [8]. The World Health Assembly in 2005, on the revision of the International Health Regulations (IHR), included dengue as a disease with the potential to emerge as a global public health emergency due to its disruptive impact and rapid epidemic spread, extending beyond national and international boundaries. Dengue is estimated to affect tens of millions of individuals each year, predominantly striking children under 15, constituting nearly 95% of the cases (7) The restricted hemodynamic capacity in young children to compensate capillary leakage could be a contributing factor to the susceptibility of young children to develop haemorrhagic shock in dengue. DENV serotypes provide lifelong serotype-specific immunity, while cross-reactive protection lasts only a few months. Subsequent infections with different serotypes may induce non-neutralizing antibodies, leading to a harmful systemic inflammatory response via antibody-dependent enhancement, which is particularly common and severe in children. The laboratory parameters, such as leukopenia and thrombocytopenia, are more pronounced in adults than in children [9]. In this study incidence were more on school going children because of the fact that they are more exposed to mosquito bite than infant, toddlers and pre-school children (see Table 1). An epidemiological study stated that Dengue symptoms vary by age, adults commonly experience myalgia, retro-orbital pain, nausea, and arthralgia, while children mainly exhibit

vomiting and petechiae. Both age groups show similar rates of fever, rash, hypotension, and diarrhoea. However, adults are more prone to leukopenia, thrombocytopenia, and elevated ALT and ESR levels [10]. DENV could directly or indirectly affect the bone marrow progenitor cells and reduce the proliferative capacity of hematopoietic cells. This virus can cause bone marrow hypoplasia. Along with platelet counts, the virus also disrupts the function of platelets due to significant deregulation of the plasma kinin system. Furthermore, DENV infection induces platelet consumption through disseminated intravascular coagulation (DIC), platelet destruction through increased apoptosis, lysis by the complement system and involvement of antiplatelet antibodies. The study also observed that the majority of cases presenting with Myalgia, gastrointestinal (GI) symptoms, and symptoms of shock were in the platelet count range of 50,000 to 100,000. Conversely, cases with platelet counts below 20,000 were notably scarce (table 3). This discrepancy may be attributed to the lack of data from patients who absconded or to the effects of early detection and management, which likely contributed to a reduction in critically low platelet counts. However, a study also suggests that in children, there is minimal correlation between platelet count and bleeding symptoms or between platelet count and disease severity. Due to a study involving 245 dengue patients, it was found that there was no apparent correlation between clinical bleeding and platelet count. Surprisingly, 81 non-bleeding patients exhibited platelet counts lower than 20,000. However, in contrast, another study involving 225 dengue patients proposed that bleeding tendencies were more frequent among patients with platelet counts below 20,000. Hence, it is recommended to administer platelet transfusions to dengue cases where platelet counts drop below 10,000-20,000 without haemorrhage or below 50,000 with bleeding or haemorrhage [11]. Despite of the fact

that platelet counts reduced in suspected cases, anaemia was not prevalent. Because the correlation between haemoglobin and platelet counts is rooted in their same origin from the bone marrow, as observed in normal adult haematopoiesis. Research indicates that a decrease in platelet levels leads to an increase in haemoglobin levels, and conversely, a decrease in haemoglobin levels is associated with a rise in platelet levels, suggesting a compensatory mechanism [12]. Accompanied by various symptoms, abdominal pain is one of the alarming signs in severe cases of dengue fever. Research indicates that a significant portion of abdominal pain cases is due to hepatitis or cholecystitis, as evidenced by elevated levels of alkaline phosphatase. The dengue virus may undergo a replication phase within hepatocytes, leading to hepatic damage, triggering apoptosis, micro vesicular steatosis, and the formation of Councilman-Rocha Lima bodies, similar to the mechanisms observed in yellow fever and other viral haemorrhagic infections. Additionally, acute abdomen can result from gastric edema and peptic ulcers, while pancreatitis and appendicitis represent rarer occurrences [13]. ELISA NS1, Rapid NS1 tests, and ELISA IgM tests were conducted on suspected dengue cases. NS1 is positive during the initial active phase of dengue infection, while IgM antibodies appear in the later phase of the illness. It was observed that patients who tested NS1 positive in the early phase presented more frequently with gastrointestinal symptoms compared to those who were IgM positive, with myalgia being common in both phases. NS1 is a glycoprotein released by infected cells and is valuable for early dengue diagnosis during the acute phase. Its specificity and high serum levels make it ideal for rapid diagnostic tests (RDTs), making it an effective tool for early detection and outbreak prevention. However, in secondary infections, the formation of antigen-antibody complexes with pre-existing IgG shortens the NS1 detection window and reduces sensitivity. This is concerning, as secondary infections are often more severe, and accurate detection is crucial for surveillance and outbreak response, particularly in dengue-endemic regions. Additionally, IgM is less than 50% sensitive at least four days after symptom onset in primary infections, limiting its utility for clinical management. Its persistence in the body for up to 60 days further complicates diagnosis in dengue-endemic regions, where antibodies from previous infections may interfere with accurate detection. Combining IgM and NS1 detection into a single test, such as the Dengue Duo kit, enhances sensitivity for both disease phases, leading to improved overall test performance [14]. This cross-sectional study provides insights into dengue-suspected cases and their diverse clinical manifestations. A longitudinal study could offer a deeper understanding of how these manifestations evolve over time, improving predictions regarding morbidity and mortality. Dengue leads to systemic changes; this study observed that, alongside severe myalgia often termed "breakbone fever". Gastrointestinal symptoms were prevalent during the acute phase. Ignoring these symptoms can result in missed diagnoses and increased severity. Additionally, dengue can affect other organs, as severe hypotension may lead to acute kidney injury, with elevated specific gravity and significant proteinuria reported in numerous studies [15]. Further research is needed to assess the extent of organ damage that may occur simultaneously during dengue infections. Moreover, collaborating with environmental scientists to study the impact

of climate change on dengue transmission dynamics and develop predictive models for outbreaks would be beneficial.

Conclusion

Dengue fever poses a significant public health challenge in India, particularly during monsoon seasons when outbreaks surge, affecting predominantly children and adolescents. The study highlights the complex interplay of factors contributing to the disease's endemicity, including urbanization, ineffective mosquito control, and climate influences. Clinical manifestations vary widely, with myalgia and gastrointestinal symptoms being prevalent, while severe cases can lead to life-threatening complications. The findings underscore the importance of early diagnosis through effective testing methods, such as NS1 and IgM detection, which are critical for timely intervention and outbreak management. By enhancing our understanding of dengue's epidemiology and clinical presentations, this research aims to inform public health strategies and improve patient outcomes in affected regions.

Abbreviation

DENV: Dengue virus, DF: Dengue Fever: DHF: Dengue Haemorrhagic Fever; DSS: Dengue Shock Syndrome; NS1 Non-Structural 1, IgM: Immunoglobulin M; ELISA: Enzyme-linked immunosorbent assay; GI symptoms: Gastrointestinal symptoms; IPD Inpatient Department; ESR: Erythrocyte Sedimentation Rate; ALT: Alanine transaminase.

Declaration

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Availability of data and materials

Data will be available by emailing dremyadav.cerum@gmail.com

Authors' contributions

Zikra Tahseen (ZT) contributed to the conceptualization, manuscript writing, and interpretation of the findings. Both authors were involved in reviewing and refining the manuscript, Chandramani Yadav (CY) was responsible for data collection, survey administration, and preliminary data analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the declaration of Helsinki. Ethical clearance was obtained from the Institutional Ethics Committee (IEC) of Autonomous State Medical College, Firozabad, -283203 (U.P), India, before the initiation of the study [Ref. No. - ASMC/IEC/2022/16 ON 19th October 2022]. Confidentiality of patient data was maintained throughout the study, and all analyses adhered to ethical research practices. Written informed consent was secured from parents or guardians of all participants.

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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