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DENGUE FEVER TRENDS AND CLINICAL VARIABILITY: A PROSPECTIVE OBSERVATIONAL STUDY FROM AYUB TEACHING HOSPITAL, ABBOTTABAD

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Abstract

Objective: This study aims to assess the clinical features, severity, and outcomes of dengue fever (DF) cases confirmed via serological testing. The research specifically focuses on patients admitted to Ayub Teaching Hospital, a tertiary care facility located in Abbottabad, Pakistan.

Methodology: This prospective observational study was conducted at Ayub Teaching Hospital, Khyber Pakhtunkhwa, Pakistan, involving 550 patients who were followed from the time of admission until discharge or death between July 2022 and July 2023. The patients were monitored, with admission criteria established based on identified warning signs. Data collection included demographic details, clinical presentation, and categorization of disease severity. Outcome measures focused on the duration of critical illness, hospital stay length, overall patient outcomes (discharge or mortality), and the evaluation of complications. The collected data were analyzed using IBM SPSS Statistics software version 22.0 (IBM Corp., Armonk, NY).

Results: The baseline characteristics of the study population indicated a male predominance of 66.8%, with a mean age of 36.77 years. Common comorbidities included hypertension (9.3%) and diabetes mellitus (7.3%). The highest prevalence of dengue fever was observed in patients with blood group B+ (15.0%). Nonstructural protein 1 (NS1) was detected in 74.4% of the cases. Fever was reported as the primary symptom in 99.0% of instances. Notable bleeding manifestations included epistaxis, gum bleeding, and hematemesis. Severe thrombocytopenia was noted in approximately 53.20% of patients at the time of admission. Hospital metrics indicated an average length of stay of 3.36 days, with a critical illness phase lasting 1.69 days, and rare complications such as expanded dengue syndrome occurring in 3.2% of cases. Remarkably, 98.9% of patients were discharged, 0.4% were transferred, and 0.7% unfortunately succumbed to the illness.

Conclusion: This study provides a detailed examination of the demographic and clinical characteristics of dengue fever (DF), highlighting a notable male predominance and fever as the most prevalent presenting symptom. The analysis indicates a relatively short duration of hospitalization, a brief critical phase, and low rates of complications. The high discharge rate reflects favorable outcomes for the majority of patients.

Keywords: dengue fever complications, dengue patient outcomes, clinical features of dengue, severe dengue manifestations, dengue infection.

Introduction

Dengue virus (DENV) remains a critical public health issue globally, affecting over 100 countries and putting nearly half of the world's population at risk. Annually, around 390 million DENV infections are reported, with a marked increase in incidence over recent decades, especially across the WHO South-East Asia region, now hyperendemic for all four DENV serotypes (DENV-1 to DENV-4)[1]. This rapid rise in dengue cases contributes significantly to regional health and economic challenges, necessitating focused research and targeted interventions a member of the *Flavivirus* genus within the *Flaviviridae* family, is a small, spherical virus with a lipid-enveloped, single-stranded, positive-sense RNA genome. The virus is predominantly transmitted by Aedes mosquitoes, including *Aedes aegypti* and *Aedes albopictus*, which thrive in tropical and subtropical regions[3]. The transmission cycle often results in shifts in the predominant DENV serotype during epidemics, correlating with increased transmission and severe disease manifestations[2].Clinically dengue infection presents a broad spectrum, from mild dengue fever (DF) to life-threatening forms involving multi-organ complications, with untreated cases facing mortality rates as high as 20%[2,5]. While a primary confers immunity to the same serotype, subsequent infections with different serotypes[4] can increase disease severity due to immunological cross-reactivity .This study examines the characteristics, disease progression, and outcomes of dengue patients admitted to Ayub Teaching Hospital. By focusing on evolving clinical parameters, it seeks to expand our understanding of this dynamic disease within a tertiary care setting and offers insights that may improve patient care and management strategies.

Materials and Methods

Study Design, Setting, and Patients; This prospective observational study was carried out at Ayub Teaching Hospital, a 1,640-bed tertiary care center in Abbottabad, Khyber Pakhtunkhwa, Pakistan. Between July 2022 and July 2023, 550 patients were observed from admission to discharge or death. Admission criteria were based on clinical identification of warning signs and severe cases. Patients exhibiting warning signs, presenting in shock, with comorbidities, or showing features of expanded dengue syndrome were included. Exclusion criteria were applied to individuals unable to communicate or unwilling to provide informed consent. All study procedures adhered to ethical research standards.

Clinical and Laboratory Investigations; Dengue fever (DF) diagnosis was determined through a combination of clinical assessments and laboratory findings. DF was suspected in cases of reported fever accompanied by at least two symptoms, including anorexia, nausea, rash, aches and pains, warning signs, leucopenia, or a positive tourniquet test. Laboratory confirmation of DF was achieved by detecting the nonstructural protein 1 (NS1) antigen or IgM antibodies using enzyme-linked immunosorbent assays (ELISA)[6].Blood samples were collected in aseptic ethylenediaminetetraacetic acid (EDTA) tubes, and IgM capture ELISA along with IgG ELISA were employed to analyze anti-dengue antibodies. Complete blood count (CBC) analysis, especially platelet count and hematocrit (HCT) levels, was conducted at baseline and every 12-24 hours based on clinical needs. Liver and renal function tests were also performed. Bleeding sites, platelet counts during episodes, and clinical manifestations of bleeding were systematically monitored. Warning signs included abdominal pain or tenderness, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, restlessness, liver

enlargement (>2 cm), and hematocrit increase with a corresponding rapid platelet count drop. Patients with these signs, shock, comorbidities, or expanded dengue syndrome were prioritized for admission.
Data Collection; Data were gathered through a structured questionnaire and managed using Microsoft Excel (Microsoft Corp., Redmond, WA) to ensure systematic and efficient data processing. Information collected included demographic details (age, gender, comorbidities, BMI, blood group, and prior dengue history). Thrombocytopenia severity was categorized as follows: mild (100,000–150,000 cells/mm³), moderate (50,000–100,000 cells/mm³), severe (20,000–50,000 cells/mm³), and very severe (<20,000 cells/mm³). Clinical data on presenting symptoms facilitated classification of symptomatic dengue virus (DENV) infections as DF or dengue hemorrhagic fever (DHF). DHF cases were further graded based on severity, with grades 3 and 4 defined as dengue shock syndrome (DSS).

DF/DHF/ DSS	Grade	Symptoms	Laboratory
DF	-	Fever with two or more signs: headache, retro-orbital pain, arthralgia, and myalgia	Leucopenia and occasional thrombocytopenia may be present. No plasma loss.
DHF	1	The abovementioned signs plus a positive tourniquet test	Thrombocytopenia ≤100,000, hematocrit rise ≥20 %
	2	The abovementioned signs plus spontaneous bleeding	Thrombocytopenia ≤100,000, hematocrit rise ≥20 %
DSS	3	The abovementioned signs plus circulatory failure, weak pulse, hypotension, and restlessness	Thrombocytopenia ≤100,000, hematocrit rise ≥20 %
	4	Profound shock with undetectable blood pressure and pulse	Thrombocytopenia ≤100,000, hematocrit rise ≥20 %

TABLE 1: Grading of dengue fever and associated laboratory parameters
DF: dengue fever; DHF: dengue hemorrhagic fever; DSS: dengue shock syndrome

Outcome Measures; The study's outcome measures were designed to capture a comprehensive assessment of clinical progress and prognosis. These included the duration of the critical phase, length of hospital stay, severity classification of dengue, final patient outcomes (discharge or death), and a detailed evaluation of complications, including rhabdomyolysis, encephalitis, hepatitis, and acute kidney injury. This approach provided a thorough understanding of the morbidity and potential risks associated with dengue fever.
Statistical Analysis; Data collected from the structured questionnaires were systematically coded and analyzed using IBM SPSS software version 22.0 (IBM Corp., Armonk, NY). Categorical variables, such as patient demographics and clinical characteristics, were represented as frequencies and percentages, while continuous variables were summarized using mean values, standard deviation (SD), interquartile range (IQR), and median, as appropriate, to ensure comprehensive data representation and facilitate accurate statistical interpretation.
Ethical Considerations; Ethical approval was secured from the institutional review board of Ayub Teaching hospital Abbottabad Pakistan (approval number: F.1-1/2022-ERB//1031), granted on July 7, 2022. Written informed consent was obtained from all participants or their legal guardians before study enrollment, ensuring adherence to ethical research principles and participant confidentiality throughout the study.

Results

TABLE 2: Baseline characteristics of the study population (N=550) N: number

Variables		N 550 (%)
Gender	Female	183 (33.2%)
	Male	367(66.8%)
Age (in years (Mean±SD))		35.77±15.26
	<30 years	248 (45.1%)
	31 to 50 years	208 (37.9%)
	51 to 70 years	84 (15.3%)
	>70 years	10 (1.8%)
BMI (kg/m2 (Mean±SD))		25.83±3.43
Comorbidities	Diabetes mellitus	40 (7.3%)
	Hypertension	51(9.3%)
	Ischemic heart disease	15(2.7%)
	Others	25 (4.6%)
Blood group	A+	57 (10.4%)
	A-	6(1.0%)
	B+	83 (15.0%)
	B-	7 (1.2%)
	AB+	19(3.4%)
	AB-	4(0.8%)
	O+	70 (12.7%)
	O-	21 (3.9%)
	Not reported	284(51.7%)

Table 2 provides an overview of the baseline characteristics of the 550 patients enrolled in the study. The cohort exhibited a male predominance, with 66.8% of the participants being male and 33.2% female.

The study population had an average age of 35.77 years (SD = 15.26), indicating a relatively young demographic. The mean body mass index (BMI) was recorded at 25.83 kg/m² (SD = 3.43), suggesting that most participants fell within the overweight range. Comorbidities were observed in the cohort, with hypertension affecting 9.3% of participants, diabetes mellitus at 7.3%, and ischemic heart disease at 2.7%. The distribution of blood types revealed that the B+ blood group was the most prevalent among the affected individuals, constituting 15.0% of the total study population.

TABLE 3: Clinical presentation and laboratory parameters of the study group

Variables		N (%)
Dengue diagnostics	IgG only	22 (4.0%)
	IgM only	39 (7.1%)
	Nonstructural protein 1 (NS1) only	404 (73.4%)
	IgG + IgM	29 (5.2%)
	IgG + NS1	03 (0.6%)
	IgM + NS1	34 (6.2%)
	IgG + IgM + NS1	14(2.6%)
	Negative	06 (1.0%)

Presenting complaints	Fever	539(98.0%)
	Nausea/vomiting	389 (70.7%)
	Abdominal pain	161 (29.3%)
	Body ache	330 (60.0%)
	Headache	134(24.3%)
	Cough	37(6.7%)
	Retro-orbital pain	34 (6.2%)
Febrile period at admission (days (Mean±SD))		4.70±2.76
Number of days at which fever is resolved (Mean±SD)		3.45±2.07
Laboratory parameters (Median (IQR))	Platelets (per µL (N=550))	M=15,000.0 (IQR=12,000.0-18,000.0)
	Creatine phosphokinase (CPK) (U/L (N=2))	M=870.0 (IQR=395.0-1345.0)
	Alanine transaminase (ALT) (U/L (N=109))	M=220.0 (IQR=98.0-342.0)
	C-reactive protein (CRP) (mg/dL (N=35))	M=220.5 (IQR=76.0-365.0)
	Total leukocyte count (TLC) (cells per µL (N=550))	M=1,809.5 (IQR=1,200.0-2,419.0)
	Hemoglobin (Hb) (g/dL (N=550))	M=8.7 (IQR=7.5-10.0)
	Hematocrit (HCT) (% (N=540))	M=24.5 %(IQR=20.0-29.0)
	Neutrophils (% (N=478))	M=73.0% (IQR=56.0-90.0)
	Lymphocytes (% (N=470))	M=6.0 %(IQR=2.0-10.0)
	Monocytes (% (N=501))	M=4.2% (IQR=1.4-7.0)

N: number; IQR: interquartile range

The predominant presenting complaint was fever (98.0%), followed by nausea/vomiting (70.7%). The mean febrile period at admission was 4.70±2.76 days

- **Mild Thrombocytopenia:** Platelet count ranges from 100,000 to 150,000 cells/mm³.
- **Moderate Thrombocytopenia:** Platelet count ranges from 50,000 to 100,000 cells/mm³.
- **Severe Thrombocytopenia:** Platelet count ranges from 20,000 to 50,000 cells/mm³.
- **Very Severe Thrombocytopenia:** Platelet count is below 20,000 cells/mm³.

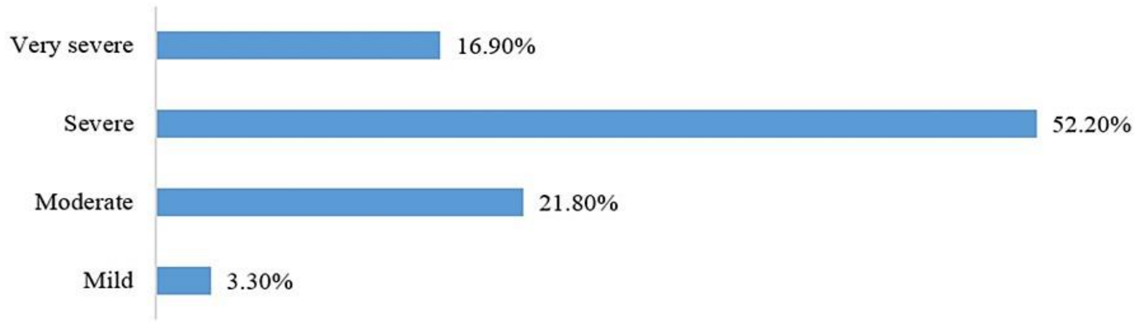


FIGURE 1: Severity of thrombocytopenia in the enrolled patients

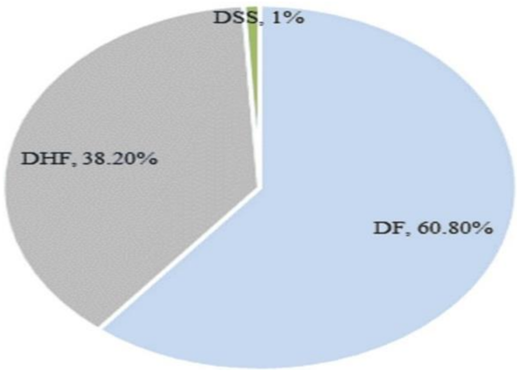


FIGURE 2: The severity of dengue fever among the study participants

DSS: dengue shock syndrome; DHF: dengue hemorrhagic fever; DF: dengue fever

Occurrence of bleeding	Site of bleeding	Frequency (%)
At admission	Bleeding per rectum (PR)	18 (3.3%)
	Hemoptysis	15 (2.8%)
	Gums	43(7.8%)
	Hematuria	25(4.5%)
	Gastrointestinal (GI) bleed	2(0.4%)
	Epistaxis	52 (9.4%)
	Bleeding per vaginum (PV)	20(3.7%)
	Melena	06 (1.1%)
	Hematemesis	17(3.1%)
During hospital stay	PV	04(0.7%)
	PR bleed	07 (1.3%)
	GI bleed	03 (0.5%)
	Gums	17 (3.0%)
	Hematemesis	07 (1.3%)
	Melena	06(1.1%)
	Hemoptysis	02(0.3%)
	Hematuria	07(1.3%)
	Epistaxis	12(2.1%)

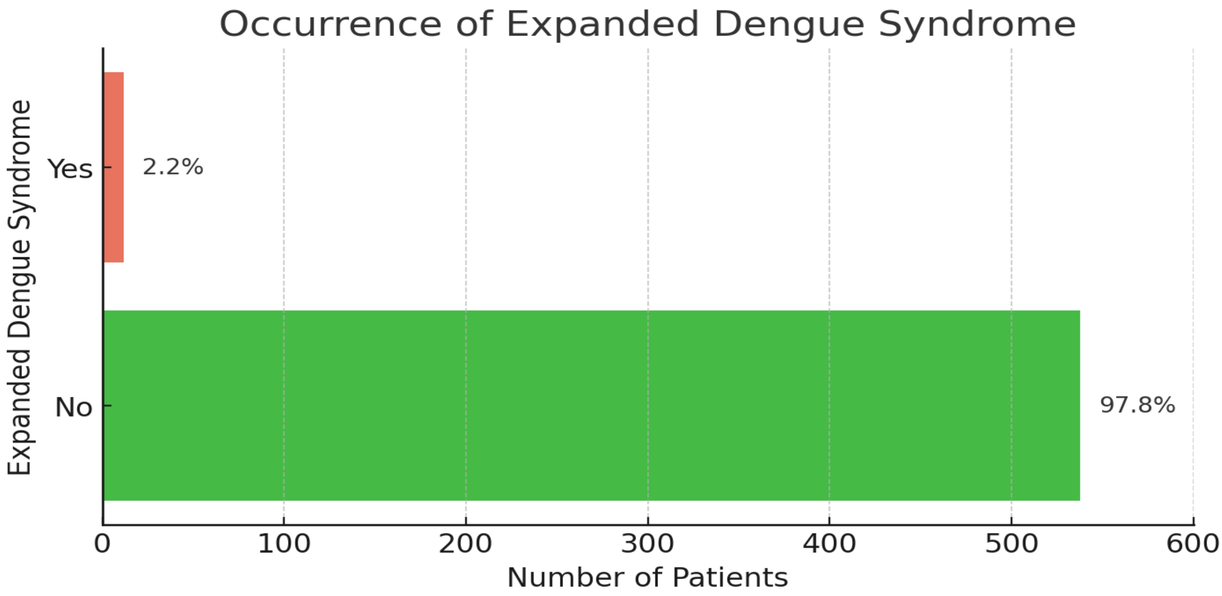
TABLE 4: Bleeding manifestations among the study participants

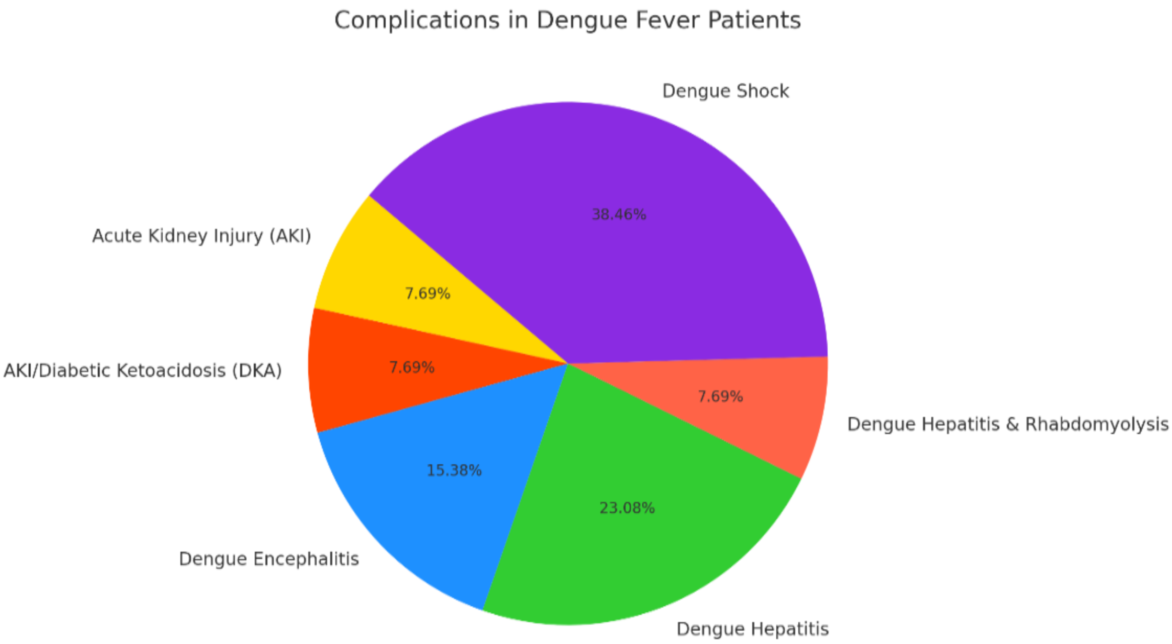
At admission, common bleeding manifestations included epistaxis (9.4%), gum bleeding (7.8%), and hematemesis (3.1%). During hospitalization, occurrences of bleeding included epistaxis (2.1%), gum bleeding (3.0%), and hematuria (1.3%).

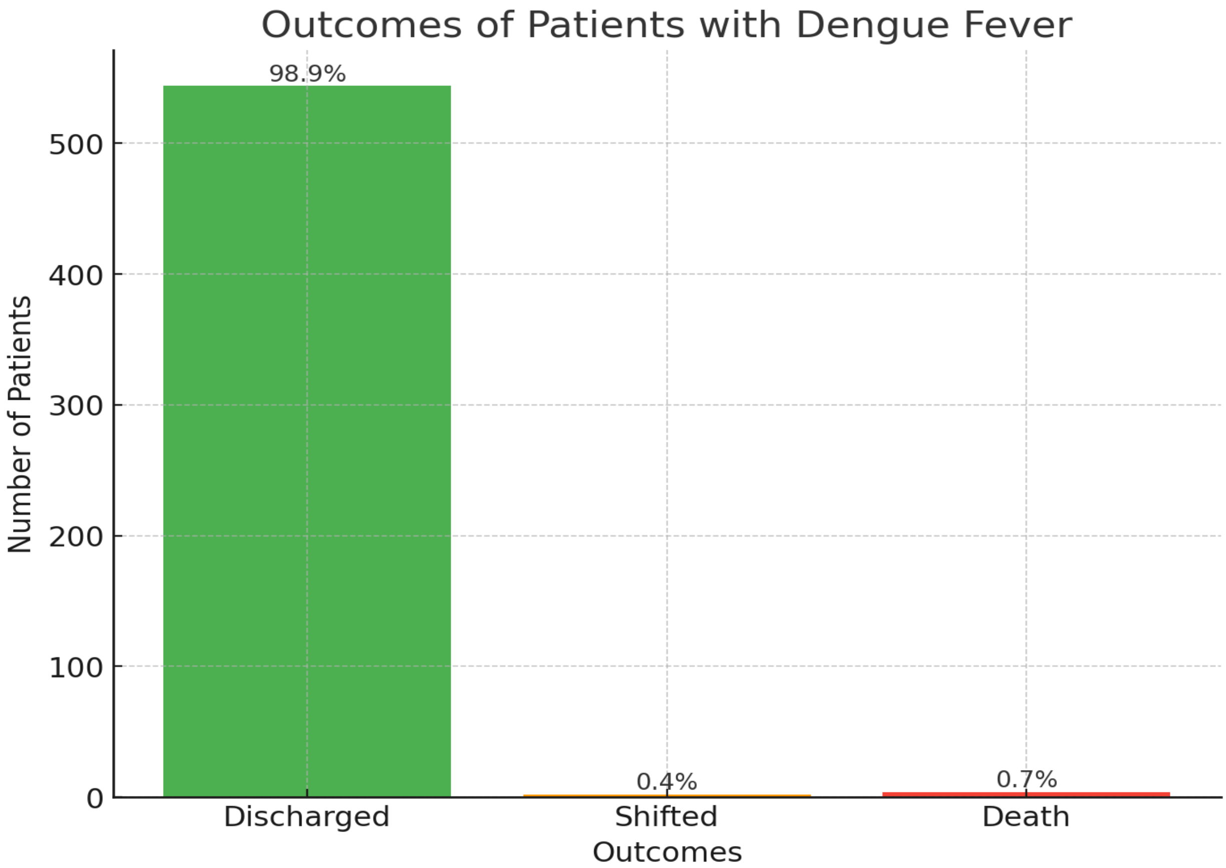
Variables		N (%)
Duration of hospital stay in days (N=550) (Mean±SD)		3.35±2.03
Duration of critical phase (N=287) (Mean±SD)		1.68±1.00
	Acute kidney injury (AKI)	0.5=1 (0.09%)
	AKI/diabetic ketoacidosis (DKA)	0.5=1 (0.09%)
	Dengue encephalitis	1.6=2 (0.29%)
	Dengue hepatitis	3.2=3 (0.59%)

Complications	Dengue hepatitis and rhabdomyolysis	1 (0.19%)
	Dengue shock	4.9=5(0.89%)
Expanded dengue syndrome	Yes	12 (2.2%)
	No	538(97.8%)
Outcomes	Discharged	544(98.9%)
	Shifted	02(0.4%)
	Death	04(0.7%)

The mean duration of hospital stay was 3.35±1.68 days for those affected. Complications were rare, with 97.8% having no complications. Encouragingly, 98.9% of patients were discharged, 0.4% were shifted, and 0.7% succumbed to the disease.







Discussion

Dengue virus infection represents a pressing global health issue, especially with severe manifestations like Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS), which put immense pressure on healthcare systems worldwide. In Pakistan, where dengue outbreaks have reached alarming levels, timely policy actions are critical to reducing associated mortality and morbidity[7].

During the 2022-23 dengue epidemic at Ayub Teaching Hospital in Abbottabad, nearly half (45.1%) of the hospitalized dengue patients were aged 30 or younger, with a mean age of 35.77±15.26 years. This aligns with previous data from a 2019 outbreak study in Rawalpindi, where the majority of cases (30.4%) were in the 31-40 age range, showing a median age of 36±14.6 years.

In terms of clinical classification, following WHO's 1997 guidelines, 60% of cases were diagnosed as uncomplicated Dengue Fever (DF), 38.2% as DHF, and only 0.9% as DSS in our hospital. These figures are consistent with other local studies, including one by Shahid et al. at Rawalpindi Medical University, which reported 54.8% of cases as DF, 43% as DHF, and 2.2% as DSS. Comparatively, a study in Malaysia following WHO's 2009 classification noted higher DF rates (88.1%) but lower rates of DHF and DSS at 11.1% and 0.8%, respectively[8]. This difference may reflect unique regional challenges in Pakistan, such as limited public health awareness, delays in seeking healthcare, and potential gaps in hygienic practices, which could contribute to a higher prevalence of severe cases.

Hospital stay duration varied widely among patients, with a mean stay of 3.35±2.03 days and a critical phase averaging 1.68±1.00 days. While a local study recorded a shorter stay of 1.28±0.67 days, our findings align more closely with the Malaysian study, where patients stayed an average of 4.88±2.74 days. Such discrepancies may stem from differences in healthcare protocols, patient management strategies, and case severity.

Clinically, fever was the predominant symptom in 98% of cases, lasting 4.70±2.76 days on average. Other common symptoms included nausea/vomiting (70.7%), abdominal pain (29.3%), body aches (60%), and headache (24.3%), while a smaller percentage reported cough (6.7%) and retro-orbital pain (6.2%). Notably, bleeding manifestations such as epistaxis, gum bleeding, and hematemesis were observed. These findings align with a study from Dhaka, which similarly reported fever as the chief symptom (94.56%), along with myalgia, rash, and bone pain, suggesting shared symptomatology across regions but with some variation in severity[7,9].

Thrombocytopenia was a prominent feature in our cohort, with severe thrombocytopenia observed in 52.2% of cases, very severe thrombocytopenia in 16.9%, moderate in 21.8%, and mild in 3.3%, while 5.7% presented with normal platelet counts. In comparison, an Indian study on children reported a higher prevalence of thrombocytopenia (92%) with varying degrees of severity, indicating possible age-related or regional differences.

Exploring blood group distribution in dengue patients revealed a potential link between blood types and disease severity. Among those who reported their blood group, 10.4% had A+, 15% B+, 12.7% O+, and smaller percentages for other groups. While previous studies have linked blood group O with severe manifestations and blood group A with a relatively lower risk, our findings indicate that group O patients were less affected by severe forms of dengue. This complex relationship warrants further investigation to better understand how host factors may influence disease severity.

Complications were relatively rare, with most patients (97.8%) experiencing none, while the few reported cases involved DSS, dengue shock, or hepatitis. Encouragingly, 98.9% of patients were discharged, with only 0.4% transferred and 0.7% succumbing to the illness. These outcomes echo similar mortality rates reported in Taiwanese studies and underscore the critical role of timely intervention in achieving favorable outcomes for dengue patients[8].Management of DF primarily entails supportive care, emphasizing hydration, pain management with acetaminophen, and avoidance of NSAIDs to reduce bleeding risk. Severe cases necessitate hospitalization for close monitoring, intravenous fluids, and possibly blood transfusions in cases of DHF or DSS. Our study highlights the importance of proactive management in reducing complications and enhancing survival rates.

This study provides valuable insights into the demographic and clinical profile of dengue cases in Pakistan, especially during the 2022-23 epidemic. Although single-centered, the findings contribute to a deeper understanding of hospitalized dengue cases and lay the groundwork for future research and intervention strategies. Further studies across diverse regions would help contextualize these findings within the broader Pakistani population, especially among those with milder cases not requiring hospitalization.

Conclusions

This study sheds important light on the demographic and clinical characteristics of dengue fever, showing a notable male predominance among cases. Fever emerged as the most frequent symptom, reflecting the typical clinical presentation of dengue in our region. Patients required an average hospital stay of 3.35 days, with the critical phase lasting around 1.68 days. Complications were uncommon, observed in only 2.2% of cases, which suggests effective management strategies in our hospital setting. The high discharge rate further highlights the generally favorable prognosis for dengue patients when prompt and appropriate care is provided. These insights not only enhance our understanding of dengue’s clinical course in the Hazara region but also underscore the importance of early diagnosis, vigilant monitoring, and supportive care in improving patient outcomes during dengue epidemics in Pakistan. Future research, especially multi-center studies, would provide broader perspectives and help strengthen dengue management protocols across diverse healthcare settings.

Additional Information

Conflicts of Interest: None

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Authors Contribution
Concept & Design of Study; Ahmad Zeb, Fazleamin, Rashid Ali
Drafting; Data Analysis; Saira Farooq, Ahmad Noor, Ahmad Zeb, Sahib Ur Rahman, Tariq Hassan, Rashid Ali
Critical Review: Muhammad Jamshed, Asifa Irfan, Zeeshan Umar
Final Approval of version; Ahmad Zeb, Fazleamin, Rashid Ali

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