

Dengue fever in paediatric oncology patients undergoing chemotherapy: A retrospective study from a tertiary care center

Wajiha Aijaz, Ammara Hameed, Ayza Farooq, Syed Habib Ahmed, Uzma Imam

Abstract

Objective: To evaluate the clinical presentation, complications and outcomes of paediatric oncology patients undergoing chemotherapy with confirmed dengue fever.

Method: The retrospective study was conducted at the National Institute of Child Health, Karachi, and comprised data from October 1, 2022, to February 28, 2024, related to paediatric oncology patients aged 1-12 years with confirmed dengue fever and haematological or solid tumour malignancies who were on active treatment. Data from medical records was categorised as demographics, clinical presentation and complications. Data was analyzed using SPSS 26.

Results: Of the 11 patients with a median age of 5.5 years (range: 3-11 years) and an interquartile range (IQR) 4 years (IQR: 4-8), 6(54.5%) were boys and 5(46.5%) were girls. Acute lymphoblastic leukaemia was the most common malignancy 7(63.7%). Dengue fever was the diagnosis in 10(90.9%) patients, while 1(9.1%) had dengue haemorrhagic fever. Common symptoms included fever 11(100%) patients, vomiting 7(72.7%) and headache 6(54.5%). Thrombocytopenia was noted in 7(72.7%) patients, pleural effusion in 2(18.2%) and pneumonia in 3(27.3%). All 11(100%) patients were treated successfully with no fatalities.

Conclusion: Early diagnosis and supportive care led to favourable outcomes even though distinguishing dengue from febrile neutropenia remains clinically challenging due to overlapping features.

Keywords: Dengue, Paediatric oncology, Chemotherapy, Retrospective studies, Febrile neutropenia, Haematological neoplasms, Pakistan. (JPMA 76: 1847; 2026)

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Introduction

The mosquito-borne dengue virus, which causes dengue fever (DF), is a danger to global health, especially in areas with tropical and subtropical temperatures. With repeated DF outbreaks in Pakistan over the past decade, it has now been given the status of an endemic disease.¹ In 2021 in Pakistan, 48,906 confirmed cases of dengue were reported, whereas in 2022, there were 41,746 confirmed cases as of October 11, 2022. This high number was a result of floods in 2022, with majority of cases seen in Sindh where the flooding was the worse.² DF is the result of infection by one of the four serotypes of dengue virus, ranging from DEN1 to DEN4. Infection with a certain serotype provides lifelong immunity against that serotype, but only partial immunity against the other serotypes. In fact, secondary infection with other serotypes increases the chance of haemorrhagic disease.³ Dengue clinical syndrome (DCS) is categorised into DF, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) based on the criteria set by the

World Health Organisation (WHO) under the 1997 classifications of DF/DHF.⁴

In paediatric cancer patients, particularly the ones receiving chemotherapy, DF manifestations may be difficult to differentiate from febrile neutropenia. Moreover, these patients may face more a prolonged course and guarded outcomes compared to the healthy population. Various studies have been conducted regarding the manifestations and outcomes of DF in healthy population.⁵ However, there is paucity of data regarding DF manifestations and outcomes in paediatric and adult oncology patients.⁶⁻⁸ Pakistan is an endemic area for DF, and paediatric oncology patient population is immunocompromised, so DF poses a great threat to this population.

To our knowledge, no data is available from Sindh and other areas of Pakistan regarding DF in paediatric oncology patients. The current study was planned to fill the gap in literature by evaluating the clinical presentation and outcomes of paediatric oncology patients on active chemotherapy with DF.

Patients and Methods

The retrospective study was conducted at the National Institute of Child Health (NICH), Karachi, and comprised data from October 1, 2022, to February 28, 2023. Using non-

Department of Paediatric Oncology, Child Aid Association, National Institute of Child Health, Karachi, Pakistan.

Correspondence: Wajiha Aijaz. e-mail: wajiha2000@gmail.com

ORCID ID: 0009-0005-0567-4447

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probability consecutive sampling technique, all patients aged 1-12 years with an interquartile range (IQR) 4 years (IQR: 4-8), diagnosed as haematological malignancy or solid tumour malignancy who were on active treatment, and had a confirmed DF diagnosis via positive non-structural protein 1 (NS-1) antigen testing were included. Patients on palliative treatment or off-treatment were excluded, and so were patients with relapsed disease. For the purpose of the study, DF diagnosis referred to patients with laboratory-confirmed diagnosis, and while symptoms overlapped with febrile neutropenia, the diagnosis was not symptom-based.

Dengue fever was diagnosed based on the positive results of NS-1 antigen because only NS-1 antigen testing facility was available at the study site. DF diagnosis was further categorised into DF, DSS and DHS based on the WHO criteria.⁴

Data was collected through the medical records and was recorded in a predesigned proforma, which had three sections. Demographic data, including age, gender, socioeconomic status (SES), area of residence, length of hospital stay (LOS), primary diagnosis, phase of chemotherapy and DF category, was recorded in the first section. Clinical presentation, including fever, vomiting, headache, periorbital pain, bleeding, abdominal pain, vital signs, bleeding at presentation, laboratory test results, including complete blood count (CBC), dengue NS-1 antigen, liver function tests (LFTs), coagulation profile, renal function tests (RFTs), and imaging results, including gall bladder wall oedema, was noted in the second section. The third section of the proforma included complications, like encephalopathy, hepatitis, fulminant hepatic failure, acute kidney injury (AKI), myocarditis, pericardial effusion (PE), pneumonia, acute respiratory distress syndrome (ARDS), refractory shock, myositis, disseminated intravascular coagulation (DIC), haemophagocytic syndrome. Besides, outcomes were also recorded in this section.

Data was analysed using SPSS 26. Mean±standard deviation was calculated for continuous variables, like age and LOS. Frequencies and percentages were calculated for categorical variables. As this was a retrospective, descriptive study, no formal sample size calculation was performed, and, therefore, no inferential tests were applied.

Results

Of the 11 patients with a median age of 5.5 years (range: 3-11 years), 6(54.5%) were boys and 5(45.5%) were girls. The initial diagnosis of the patients were precursor B-acute lymphoblastic leukaemia 5(45%), T-cell acute lymphoblastic leukaemia 2(18.2%) and 1(%) each of Ewing sarcoma, Wilm's tumour, Hodgkin lymphoma and osteosarcoma. DF was the diagnosis in 10(90.9%) patients,

while 1(9.1%) had DHF.

Majority of the patients 8(72.7%) had a poor SES, followed by 2(18.2%) with a fair, and 1(9.1%) with extremely poor SES. Common symptoms included fever 11(100%), vomiting 7(72.7%) and headache 6(54.5%). Thrombocytopenia was noted in 7(72.7%) patients, PE in 2(18.2%) and pneumonia in 3(27.3%) (Table).

Periorbital pain was observed in 10(90.9%) patients, 8(72.7%) showed clinical manifestations of bleeding, and 6(54.5%) complained of abdominal pains. None of the patients presented with skin rashes (Figure 1).

Table: Clinical profile of paediatric oncology patients with dengue fever (n=11).

Clinical characteristics	n (%)
Tachycardia	6(54.5)
Hypotension	1(9.1)
Tachypnoea	2(18.2)
Anaemia (haemoglobin [Hb] <10g/dl)	7(63.6)
Neutropenia	5(45.5)
Thrombocytopenia	8(72.7)
Coagulation studies (deranged)	6(54.5)
Ascites (On ultrasound)	2(18.2)
Gall bladder wall oedema (on ultrasound)	2(18.2)
Hyponatraemia	3(27.3%)
Disseminated intravascular coagulation (DIC)	1(9.1)

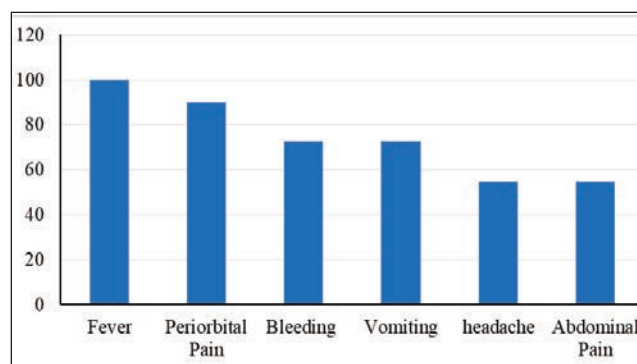


Figure-1: Presenting symptoms among the patients.

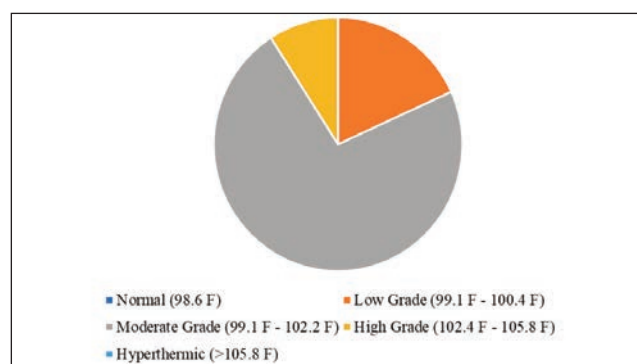


Figure-2: Characteristics of fever in the paediatric oncology patients with dengue fever.

Discussion

DF poses a great threat to individuals in an endemic area, with paediatric oncology patients being more vulnerable to complications and poor outcomes due to their already weak immune system. Strong suspicion and early identification of the presenting symptoms can aid in making an early diagnosis.

Most of the patients in the current study had the primary diagnosis of acute leukaemia. Since acute leukaemia is the commonest paediatric malignancy and the treatment is intensive as well, therefore, this could be the cause behind DF. In a study conducted in India, similar results were seen with 7(62%) of the patients having primary diagnosis of acute leukaemia⁹ and similar to the healthy population, fever was present in all the patients presenting with DF.¹⁰ In paediatric malignancy patients, a DF diagnosis is usually delayed as usual bacterial and fungal infections are considered more likely to cause infections. Such findings were observed in an Indian study in paediatric oncology population.¹¹ Moreover, DF can coexist with other infections as well.

Un the current study, DF was the most common diagnosis, with DHF diagnosed in only 1(9.1%) patient. No instances of DSS was found. This contrasts with earlier studies which reported higher incidence of DSS, including 39.1%, 22% and 33%.¹²⁻¹⁴ The key characteristic of dengue is increased vascular permeability, resulting in plasma leakage from blood vessels, which can lead to haemoconcentration, low blood pressure and shock. This may also be accompanied by haemostatic irregularities, such as low platelet count, vascular changes and coagulopathy.

In one study,¹² a change in haematocrit of >20% and the standard haematocrit thresholds established by Gomber et al.¹⁵ and Balasubramanian et al.¹⁶ were utilised as markers of haemoconcentration to diagnose and track severe dengue infection. In 6(54.5%) of the cases, the coagulation profile was abnormal, indicating that factors beyond thrombocytopenia, such as platelet dysfunction, consumption coagulopathy, and endothelial dysfunction, contributed to bleeding in DF. Neurological symptoms in dengue can include seizures, encephalopathy, acute disseminated encephalomyelitis, and, on rare occasions, Guillain-Barré syndrome (GBS). These symptoms may arise due to cerebral hypoperfusion, cerebral oedema, direct neurotropic effects, or from complications of hepatic dysfunction and metabolic imbalances, such as hypoglycaemia and hyponatraemia, as noted in previous studies.^{13,15} In the current study, no case of encephalopathy was found compared to 66% reported earlier.¹²

In DF, the causes of liver dysfunction typically involve direct

damage to liver cells, an uncontrolled immune response from the host, ongoing viral replication, and oxygen deprivation along with tissue damage due to extended shock, bleeding and acid build-up in the body. Hepatic dysfunction was observed in 1(9.1%) of the current patients compared to 11.1% reported by Pothapregada et al.¹³ In the study by Pothapregada et al., two children experienced fulminant hepatic failure, but the current study did not observe any such case. Unusual gastrointestinal complications in the current study included gallbladder wall oedema found on ultrasound in 2(18.2%) cases, and ascites in 2(18.2%). Additionally, PE was present in 2(18.2%) cases, and pneumonia was reported in 3(27.3%). The current study did not observe any instances of pericardial effusion, myocarditis or AKI.

There were no deaths in the current study compared to a mortality rate of 2.3% reported by Pothapregada et al.¹³ The common factors might include heightened public awareness, improved parental health-seeking behaviour, early detection and prompt treatment in the study, and a shift in the pattern of the epidemic's presentation compared to previous years.¹²

The current study has several limitations. Resource limitations prevented the researchers from incorporating dengue testing as a standard part of evaluating patients with febrile neutropenia. Additionally, the study could not compare the dengue NS-1 antigen test with immunoglobulin G (IgG) and IgM antibody tests because of the absence of necessary facilities. Finally, the small sample size of 11 patients limits the generalisability of the findings, which reflects the rarity of dengue co-infection in this patient population. Larger prospective studies are needed to validate the current findings and better characterise the clinical course of DF in paediatric oncology patients. To lower fatality and morbidity from the evolving epidemic pattern, clinical vigilance, knowledge of the patients, and prompt case discovery must be ensured.

Conclusion

Early diagnosis and supportive care led to favourable outcomes even though distinguishing dengue from febrile neutropenia remains clinically challenging due to overlapping features.

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Author Contribution:

WA: Concept, data collection, literature research, drafting, revision and writing.

AH: Data collection, literature research, drafting, revision, writing and editing.

AF: Data collection, drafting, revision and writing.

SHA: Literature research and final approval.

UI: Concept, revision, editing and final approval.