International Journal of Contemporary Pediatrics
Johnson DJ et al. Int J Contemp Pediatr. 2024 Jun;11(6):804-811
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20241368

Original Research Article

A study of morbidity and mortality markers in children diagnosed with severe dengue illness at a quaternary paediatric intensive care unit

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Received: 25 April 2024
Accepted: 16 May 2024

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ABSTRACT

Background: To identify the biochemical, haematological, and serological laboratory parameters and establish associations between mortality risk and children with severe dengue fever (DF).
Methods: This retro-prospective study included 251 children who were dengue serology positive, aged between 1 month and 18 years, hospitalized in paediatric intensive care unit (PICU) with severe dengue illness from July 2019 to June 2021. Clinical, laboratory, and radiological data were extracted from hospital's electronic database and analyzed.
Results: The majority had a mean age of 5.46 years with a significant female predominance (58.2%). Also, 80.1 per cent of children presented in the critical phase with an average PICU stay of 3.59 days. There was a significant mortality risk associated with presenting day of illness (risk 9.5%), ventilation requirements (risk 29.8%), and stay of more than a week in the PICU (risk 36%), with that of the severity of outcomes. The odds of increased mortality risk were associated with prolonged PICU stay exceeding a week and ventilation requirements by 10.03 and 20.19 times respectively. Investigation-wise, abnormal liver enzymes on admission such as SGOT (OR 5.39, $p>0.0001$); and serum SGPT (OR 5.54, $p<0.001$) were significantly associated with poorer outcomes. Interestingly, neither thrombocytopenia nor leucopenia was found to be a true marker of mortality and the overall mortality rate was found to be 8.4% (n=21).
Conclusions: Any stay of more than a week, abnormal liver enzymes on admission, and ventilation requirements were all associated with higher mortality risk and potential predictors for poor clinical outcomes in the PICU.

Keywords: Severe DF, Paediatric ICU, Mortality risk

INTRODUCTION

Dengue haemorrhagic fever (Philippine, Thai, or Singapore haemorrhagic fever; haemorrhagic dengue; acute infectious thrombocytopenic purpura) is a severe, often fatal, febrile disease caused by one of four dengue viruses of the genus *Flavivirus*, family *Flaviviridae*. The disease is characterized by biphasic fever, capillary permeability, abnormalities of haemostasis, and in severe cases, a protein-losing shock syndrome (dengue shock syndrome), which is thought to have an immunopathologic basis and may be associated with haemorrhagic manifestations. In 10-20% of cases, the patient develops shock because of plasma leakage into the third space. Worldwide, children younger than 15 years comprise 90% of patients with DF. A revised case definition adopted by the World Health Organization (WHO) in 2009 of severe dengue includes cases accompanied by fluid loss leading to shock or respiratory distress, liver damage as evidenced by elevations in

serum glutamic oxaloacetic transaminase (SGOT) or serum glutamic pyruvic transaminase (SGPT) levels to >1000 u/l, severe bleeding, and altered consciousness or significant heart abnormalities.[1]

DF remains a pervasive health concern, prevalent in over 100 nations, with most reported instances emanating from the Americas, Southeast Asia, and the Western Pacific regions as delineated by the WHO.[2] Within the Indian subcontinent, the endemicity of dengue is widespread, permeating virtually all states and standing as a primary causative factor necessitating hospitalization for many. Historically, DF was predominantly associated with urban locales; however, recent trends indicate its emergent presence in peri-urban and rural regions as well.[3]

The Indian health surveillance infrastructure for DF is meticulously orchestrated through a robust framework encompassing more than 600 sentinel hospitals, all operating under the aegis of the national vector borne disease control program (NVBDCP).[4] Additionally, the integrated disease surveillance program (IDSP) plays a pivotal role, alongside a specialized network of 52 virus research and diagnostic laboratories (VRDL) instituted by the department of health research.[5]

Statistical data underscores the gravity of the situation; for instance, in 2010 alone, an alarming estimation approximated a staggering 33 million dengue cases within India's borders.[6] Subsequently, by 2016, the NVBDCP registered an excess of 100,000 laboratory-confirmed dengue cases, thereby illuminating the potential discrepancy between reported and actual incidences. Given these figures, there exists a plausible contention that the true magnitude of the dengue disease burden in India might be significantly under-represented. The disease in India is prevalent in most metropolitan cities and towns, with frequent outbreaks of disease, and case fatality rates as high as 3-5%.[7]

There is no specific antiviral therapy for dengue with the mainstay of therapy being supportive and symptomatic with intravenous fluids and electrolytes management. Hence, diagnosis and intervention with close monitoring can reduce the mortality to <1%. However, mortality can reach as high as 30% if left untreated.[7] There are atypical forms of dengue infection such as hepatic dysfunction, raised total bilirubin, disseminated intravascular coagulation and electrolyte disturbances, having a profound effect on multiple organ systems; the commonest being the liver, starting from asymptomatic elevated transaminase levels to acute liver failure.[8] The median SGOT and SGPT level values are much higher for severe forms of disease and higher levels of SGOT are more common than that of SGPT, which differentiates from other forms of viral hepatitis.[9] Also, leucopenia and low platelet count are associated with the severity of the disease.[10,11] It is also found that the presence of combined dengue immunoglobulin M (IgM) or immunoglobulin G (IgG) antibodies is associated with more severe infection than the presence of either one.[10]

With the above background, the study aimed to identify crucial laboratory parameters for predicting the severity and mortality in children with severe dengue illness within a PICU setting.

METHODS

Study area

The research was carried out at a level IV quaternary PICU, Rainbow Children's hospital and perinatal centre, Banjara Hills, Hyderabad which is a 250-bed tertiary paediatric care facility offering diverse paediatric subspecialties within the state of Telangana, India.

Study design and population

This investigation employed both retrospective and prospective observational study designs. The retrospective data encompassing all children meeting the specified inclusion and exclusion criteria was gathered precisely from July 1st, 2019 to November 4th, 2020, combined with the prospective component, which included data on all children admitted after obtaining consent from November 5th, 2020 to June 30th, 2021.

Study duration

The retrospective phase of the study covered the period from July 2019 to October 2020, while the prospective phase spanned from November 2020 to June 2021.

Inclusion criteria

Data from patients meeting all the specified inclusion criteria will be incorporated into the analysis: Admission to the PICU with severe illness from July 2019 to June 2021, all children diagnosed with positive dengue serology and ages ranging from 1 month to 18 years.

Exclusion criteria

Patients meeting any of the outlined exclusion criteria will be excluded from the study: Children with pre-existing liver disease, individuals admitted before or after the specified study period, dengue patients not requiring hospitalization, immunocompromised children. Those taking medications that may impact platelet count or function, such as antiplatelet and anticoagulants.

Data collection

The commencement of the study occurred with sample size calculated and data entered accordingly based on any child exhibiting any combination of symptoms or signs of severe DF. High-grade fever, erythematous maculopapular rash, myalgia, abdominal pain, vomiting,

tachycardia, delayed capillary refill time, decreased pulses, tender hepatomegaly, ascites, pleural effusion, or bleeding manifestations, and originating from endemic areas in Hyderabad, Telangana, India, was considered as clinical features for severe dengue in the study. These children underwent assessment for elevated haematocrit, leucopenia, or thrombocytopenia, which was subsequently confirmed by positive dengue serology and were diagnostically confirmed by Non-structural protein 1 (NS1) antigen, DENG IgM and DENG IgG antibodies (Pan bioDengue Early ELISA, Standard Diagnostic Inc, Republic of Korea). Those hospitalized in the PICU due to severe illnesses stabilized with initial therapy, and meeting the criteria outlined by the WHO in 2009 were included in the study. Clinical profiling and in-house laboratory investigations were conducted, and patients were managed by hospital protocols.

Data entry and analysis

The information for the current investigation was gathered from hospital records, utilizing a pre-designed study proforma. Rigorous scrutiny was applied to ensure the completeness and consistency of the collected data. Subsequently, the information was entered into MS office excel, and a statistical analysis was carried out using SPSS (Statistical Package for the Social Sciences) version 21.

By examining various clinical variables, including days of illness, duration of PICU stay, ventilation (non-invasive as well as invasive) requirements, and levels of SGOT and SGPT, the research sought to establish associations between these factors and adverse clinical outcomes. Categorical variables were expressed in terms of frequency and percentage. To compare continuous variables between groups, an independent sample t-test was employed. For the comparison of categorical variables between groups, both the Pearson Chi-square test and Fisher's Exact test were utilized. Pearson correlation (R value) was employed to assess the correlation between variables.

RESULTS

Table 1 presents the key continuous variables describing the study population where the data represented is defined by mean with standard deviation (Mean ± SD) as well as median values using interquartile range (IQR). The average age of the participants was 5.46 years, with an average duration of 3.59 days in the PICU. The mean levels of SGOT and SGPT were 1140.94 U/L and 353.72 U/L, respectively. Additionally, the mean values for prothrombin time (PT) and activated partial thromboplastin time (APTT) at 22.39 seconds and 64.33 seconds, respectively. The mean packed cell volume (PCV) was recorded as 33.83%.

Table 2 presents the general characteristics of a study population comprising 251 individuals, emphasizing categorical variables which are expressed in frequency (n) and percentage (%). Notable observations include a gender distribution with 41.8% males and 58.2% females. Most patients (80.1%) experienced the critical phase of illness, while 43.4% had a PICU stay lasting 3 to 7 days. Ventilation was administered to 22.7% of individuals, and the overall clinical outcome exhibited an 8.4% mortality rate. Most tested positive for dengue Ig M (88.8%), and dengue Ig G (54.2%) antibodies. A significant proportion had mild to severe elevation in SGOT (48.2% to 19.9%) and SGPT (45.8% to 12.4%) levels on admission. Serum albumin levels below three grams per decilitre were observed in 76.5% of cases, while severely low platelet counts were noted in 60.2% cases. Leucocytosis and leucopenia were observed only in 19.9% of each, whereas 90.8% and 91.6% of patients did not have encephalopathy or bleeding respectively. These findings collectively contribute to the characterization of the study population and provide a foundation for understanding the distribution of key categorical variables about clinical outcomes.

Table 3 outlines the association between various risk factors and clinical outcomes in a study population of 251 individuals. $p<0.001$ was taken to be significant. Notable findings include a significant association between the number of days of illness in the critical phase and clinical outcomes ($p=0.124$), with 9.5% mortality during this phase. The duration of PICU stay is strongly correlated with outcomes ($p<0.0001$), revealing a mortality rate of 36.0% for patients admitted more than week. Ventilation requirement is significantly linked to poor outcomes ($p<0.0001$) with a mortality rate of 29.8%. Liver function markers (SGOT and SGPT) on admission also demonstrate significant associations with poor outcome ($p<0.0001$), with severe elevation showing higher mortality rates whereas leucocytosis ($p=0.001$) and presence of encephalopathy ($p=0.421$) are associated with varying clinical outcomes. Bleeding tendencies show trend towards significance ($p=0.084$). Study employs Fisher exact and Chi-square tests for statistical analysis, providing comprehensive insight into relationship between these variables and clinical outcomes in studied population.

Table 4 presents the results of bivariate logistic regression analysis for predictor variables in a study population of 251 individuals. $p<0.001$ was taken to be statistically significant. Notably, odds of experiencing the critical phase of dengue illness are 2.5 times higher, although this association is not statistically significant ($p=0.227$). However, number of days in PICU exceeding a week significantly increases odds of adverse outcomes by 10.031 times, and ventilation requirement is associated with substantial increase in odds by 20.187 times. Severely elevated levels of SGOT and SGPT both demonstrate significant associations with adverse outcomes, with OR of 5.387 and 5.538, respectively. Platelet deficiency and leucopenia did not show statistically significant associations with adverse

outcomes. Adjusted odds ratios and confidence intervals were also reported, providing further insights into strength and precision of these associations. These findings underscore importance of PICU stay duration, ventilation requirement, and elevated liver enzyme levels as potential predictors for adverse clinical outcomes in studied population.

Table 1: General characteristics (continuous variables) of the study population, (n=251).

Variables	Mean ± SD	Median (IQR)
Age (in years)	5.46±4.678	4 (1 to 10)
SOFA[$] score	4.29±2.859	3 (3 to 5)
Number of days of PICU stay	3.59±3.014	3 (2 to 4)
SGOT	1140.94±2597.87	244 (136 to 740)
SGPT	353.72±635.54	100 (50 to 284)
Serum albumin	2.441±0.66	2.5 (2 to 2.9)
PT	22.39±17.54	18 (16 to 22)
APTT	64.33±27.3	58 (42 to 78)
Platelet count	65733.07±72710.03	41000 (25000 to 69000)
Haemoglobin	11.17±2.71	11.5 (9.4 to 13.2)
PCV	33.83±7.72	34.1 (29.4 to 39)
WBC count	9076.43±6014.68	7620 (5470 to 10770)

$SOFA-Sequential organ failure assessment scoring done at time of admission, SGOT-Serum glutamic oxaloacetic transaminase, SGPT-Serum glutamic pyruvic transaminase, PT-Prothrombin time, APTT-Activated partial thromboplastin time, PCV-Packed cell volume, WBC-White blood count.

Table 2: General characteristics (categorical variables) of the study population, (n=251).

Variables		N	Percentage (%)
Gender	Male	105	41.8
	Female	146	58.2
Day of Illness[^]	Critical phase[€]	201	80.1
	Febrile phase	32	12.7
	Resolution phase	18	7.2
Number of days of PICU stay	3 to 7 days	109	43.4
	Less than or equal to 2 days	117	46.6
	More than a week	25	10.0
Ventilation given[Ω]	No	194	77.3
	Yes	57	22.7
Clinical outcome	Death	21	8.4
	Discharge	230	91.6
Non-structural protein-1 antigen	Negative	197	78.5
	Positive	54	21.5
Dengue immunoglobulin M	Negative	28	11.2
	Positive	223	88.8
Dengue immunoglobulin G	Negative	115	45.8
	Positive	136	54.2
Both dengue immunoglobulin M and immunoglobulin G	Negative	129	51.4
	Positive	122	48.6
SGOT on admission[£12]	Mild elevation	121	48.2
	Moderate elevation	71	28.3
	Normal	9	3.6
	Severe elevation	50	19.9
SGPT on admission[£12]	Mild elevation	115	45.8
	Moderate elevation	39	15.5
	Normal	66	26.3
	Severe elevation	31	12.4
Serum albumin	Less than 3 mg/dL	192	76.5
	More than or equal to 3	59	23.5
Platelet count[*13]	Mild deficiency	16	6.4

Continued.

Variables		N	Percentage (%)
	Moderate deficiency	58	23.1
	Normal	26	10.4
	Severe deficiency	151	60.2
WBC count#	Leucocytosis	50	19.9
	Leukopenia	50	19.9
	Normal	151	60.2
Encephalopathy	Absent	228	90.8
	Present	23	9.2
Bleeding**	Absent	230	91.6
	Present	21	8.4

^Presenting day at admission calculated from symptom onset, Ω Mode of ventilation non-invasive and invasive both were used, $ as tested by Pan bio dengue serology kit, £ for both SGOT and SGPT levels; Normal: ≤50 U/L, mildly elevated: 51-250U/L, moderately elevated: 251-499U/L, severely elevated: ≥500U/L. *Normal platelet count: ≥150000 cells/mm^3, mild deficiency: 70000-150000 cells/mm^3, moderate deficiency: 20000-50000 cells/mm^3, severe deficiency: ≤20000 cells/mm^3, # Normal WBC count: 4000-12000 cells/mm^3, Leucopenia: ≤4000 cells/mm^3, Leucocytosis: ≥12000 cells/mm^3, **Any minor bleeding (petechial or purpuric rash, gum bleed, epistaxis) or major bleeding (haematemesis, haematochezia, melaena, haemoptysis or intracranial bleed). € Febrile phase of dengue (according to WHO 2009 definition): Day 1-4, Critical phase: Day 3-7, resolution phase: Day 7 onwards.

Table 3: Association between risk factors and clinical outcome of the study population, (n=251).

Variables			Clinical outcome		Total	P value**
			Death	Discharge		
Day of illness^	Critical phase€	Count (n)	19	182	201	0.124*
		%	9.5	90.5	100	
	Febrile phase	Count (n)	0	32	32	
		%	0.0	100	100	
	Resolution phase	Count (n)	2	16	18	
		%	11.1	88.9	100	
Number of days of PICU stay	3 to 7 days	Count (n)	7	102	109	<0.0001#
		%	6.4	93.6	100	
	Less than or equal to 2 days	Count (n)	5	112	117	
		%	4.3	95.7	100	
	More than a week	Count (n)	9	16	25	
		%	36	64	100	
Ventilation given	No	Count (n)	4	190	194	<0.0001*
		%	2.1	97.9	100	
	Yes	Count (n)	17	40	57	
		%	29.8	70.2	100	
Both Ig M and Ig G	Negative	Count (n)	11	118	129	0.925#
		%	8.5	91.5	100	
	Positive	Count (n)	10	112	122	
		%	8.2	91.8	100	
SGOT on admission£12	Mild elevation	Count (n)	1	120	121	<0.0001*
		%	0.8	99.2	100	
	Moderate elevation	Count (n)	9	62	71	
		%	12.7	87.3	100	
	Normal	Count (n)	0	9	9	
		%	0.0	100	100	
	Severe elevation	Count (n)	11	39	50	
		%	22.0	78	100	
SGPT on admission£12	Mild elevation	Count (n)	5	110	115	<0.0001*
		%	4.3	95.7	100	
	Moderate elevation	Count (n)	7	32	39	
		%	17.9	82.1	100	
	Normal	Count (n)	1	65	66	
		%	1.5	98.5	100	
	Severe elevation	Count (n)	8	23	31	
		%	25.8	74.2	100	
Serum albumin	Less than 3	Count (n)	16	176	192	1.000*

Continued.

Variables			Clinical outcome		Total	P value**
			Death	Discharge		
		%	8.3	91.7	100	
	More than or equal to 3	Count (n)	5	54	59	
		%	8.5	91.5	100	
Platelet count[¥ 13]	Mild deficiency	Count (n)	0	16	16	0.242*
		%	0.0	100	100	
	Moderate deficiency	Count (n)	6	52	58	
		%	10.3	89.7	100	
	Normal	Count (n)	0	26	26	
		%	0.0	100	100	
	Severe deficiency	Count (n)	15	136	151	
		%	9.9	90.1	100	
WBC count[Ω]	Leucocytosis	Count (n)	9	41	50	0.001*
		%	18	82.0	100	
	Leucopenia	Count (n)	7	43	50	
		%	14.0	86.0	100	
	Normal	Count (n)	5	146	151	
		%	3.3	96.7	100	
Encephalopathy	Absent	Count (n)	18	210	228	0.421[#]
		%	7.9	92.1	100	
	Present	Count (n)	3	20	23	
		%	13.0	87.0	100	
Bleeding**	Absent	Count (n)	17	213	230	0.084[#]
		%	7.4	92.6	100	
	Present	Count (n)	4	17	21	
		%	19.0	81.0	100	

*Obtained by using Fischer's exact test, #Obtained by using Chi-square test, **p<0.001 was taken to be statistically significant, ^Presenting day of dengue illness calculated from symptom onset, € According to WHO 2009 definition-Febrile phase of dengue (Day 1-4, Critical phase: Day 3-7, Resolution phase: Day 7 onwards. £for both SGOT and SGPT levels; Normal: ≤50 U/L, mildly elevated: 51-250U/L, moderately elevated: 251-499U/L, severely elevated: ≥500U/L, ¥ Normal platelet count: ≥150000 cells/mm^3, mild deficiency: 70000-150000 cells/mm3, moderate deficiency: 20000-50000 cells/mm^3, severe deficiency: ≤20000 cells/mm^3, Ω Normal WBC count: 4000-12000 cells/mm^3, Leucopenia: ≤4000 cells/mm^3, Leucocytosis: ≥12000 cells/mm^3, **Any minor bleeding (petechial or purpuric rash, gum bleed, epistaxis) or major bleeding (haematemesis, haematochezia, melaena, haemoptysis or intracranial bleed). PICU-Paediatric intensive care unit, IgM-dengue Immunoglobulin M antibody, Ig G-dengue Immunoglobulin G antibody, SGOT-serum glutamic oxaloacetic transaminase, SGPT- serum glutamic pyruvic transaminase, WBC-White blood cell.

Table 4: Bivariate logistic regression analysis between predictor variables, (n=251).

Predictor variables for mortality risk	Indicator	OR	P value*	Adjusted OR	95% CI for adjusted OR	
					Lower	Upper
Day of illness[£]	Critical phase[€]	2.5	0.227	6.051	1.089	33.633
No. of days of PICU stay	More than a week	10.031	<0.0001	4.336	1.166	16.115
Ventilation	Given[∑]	20.187	<0.0001	18.018	4.194	77.415
SGOT	Severely elevated[$]	5.387	<0.0001	1.509	0.293	7.782
SGPT	Severely elevated[$]	5.538	0.001	1.134	0.195	6.593
Platelet	Severe deficiency [Ω]	1.728	0.275	0.739	0.212	2.579
WBC count	Leukopenia[¥]	2.174	0.115	6.501	1.640	25.766

*P<0.001 is taken as statistically significant, £ Presenting day at admission calculated from symptom onset, € Critical phase of dengue-day 3 to day 7, ∑-Both invasive and non-invasive modes of ventilation were given, $-SGOT and SGPT levels severely elevated=≥500U/L, Ω-Platelet severe deficiency=≤20000 cells/mm^3, ¥-Leucopenia=≤4000 cells/mm^3

DISCUSSION

In our research, we determined that the average age of the individuals involved in the study was approximately 5.46 years old. A significant portion of these participants were females, making up 58.2% (n=146) of the total. In contrast to our study, research conducted by Mishra et al in Odisha, India revealed different findings. Their study reported that average age of participants was 8.7 years.[14]

In contrast to both our study and the research conducted by Mishra et al a study conducted by Soomar et al in Pakistan indicated that the primary age group of

participants who tested positive for dengue was between 13 to 18 years old.[15] Another study conducted by Islam et al and Mutanabbi et al both in 2022 in Bangladesh, showed the mean age of the participants in their study was 7.3 years and 6.95 years respectively, however, both their research also contradicted our findings and noted a male majority.[16,17] These discrepancies could potentially be attributed to variations in the study populations.

Our study found that the mean SOFA scores were highest for the first 24 hours of PICU admission i.e. 4.29 which meant average patients included in the study were sick. This coincided with the finding that a striking 80.1% (n=201/251) of the patients were hospitalized during the critical phase of dengue illness and this was similarly echoed in studies done by Mishra et al in Odisha, India and Nagaram et al in Andhra Pradesh, India which showed dengue children each getting admitted with an average of 5 days before onset of their symptoms.[14,18] Also noted upon admission, 19.9% (n=50) of the patients exhibited a severe increase in SGOT levels (only 3.6% or 9 cases had normal levels), while 12.4% (n=31) showed a pronounced rise in SGPT levels. Out of 251 children enrolled in the study, 10% (n=25) required an extended stay of more than a week in the PICU and the majority of them (53.4%, n=134) required a stay of more than 3 days. This was supported by a similar study done by Raju et al in Karnataka, India reported that 78.6% of children with more than three times elevated SGPT levels, and 60 per cent of children with more than six times elevated SGOT levels had more than 6 days of hospital stay also thereby, predicting disease severity and fatal outcomes.[19]

On top of that, the elevation of mean SGOT levels was significantly higher compared to mean SGPT levels. This was comparable to a study done by Zubair et al and Mishra et al who showed that the median SGOT and SGPT level values are much higher for severe forms of dengue disease and that higher levels of SGOT are more common than for SGPT, which differentiates from other forms of viral hepatitis and attributable to increased involvement of myocytes. SGOT value of more than 1000 IU/L indicates the severity of the disease along with morbidity and mortality.[7,9] Additionally, the study done by Mishra et al observed an elevation in SGOT levels in 47.4% of the cases studied.

Furthermore, thrombocytopenia in this study was identified in 27.5% of cases. The prevalence of mortality among dengue patients stood at a relatively lower rate of 1.3% in stark contrast to the mortality rate presented in our study which was 8.4% (n=21/251 cases).[14] This difference needs further research. Also, our findings revealed a significant 89.7% (n=225) of the patients exhibited thrombocytopenia. Interestingly, a study conducted by Islam et al in Bangladesh and Nagaram et al in South India mirrored our findings, with 42 and 53% of their cases displaying thrombocytopenia.[16,18]

Respiratory complications in severe dengue need ventilator support as a part of management, which was required in 22.7% (n=57) of patients. Various invasive modes (pressure-regulated volume control or PRVC, synchronized intermittent mandatory ventilation or SIMV and high-frequency oscillatory ventilation or HFOV) as well as non-ventilation modes (continuous positive pressure ventilation or CPAP, heated humidified high-flow nasal cannula or HHHFNC) were used for the admitted patients and ventilation used was significantly linked to adverse outcomes with mortality rate of 29.8% (n=17/251) for 57 ventilated individuals. Moreover, 9% (n=23) of participants experienced encephalopathy as a complication, and eight per cent (n=21) developed bleeding manifestations during their course in PICU. In a study conducted by Yesmin et al observed notably higher prevalence of bleeding manifestations, specifically at 17%.[20] In contrast, in the study conducted by Mutanabbi et al it was noted at 29.4%.[17] Such significant difference in findings compared to other studies, including ours, might be attributed to variations in sample sizes and can indeed influence observed prevalence rates and necessitate careful considerations when interpreting and comparing study outcomes.

In our research, based on bivariate logistic regression studies, we discovered that there was no notable association between a patient's death and their admission during the critical phase of their illness days. However, we did identify a significant association between a patient's death and their prolonged stay of over a week in PICU (OR 10.031, $p<0.0001$). Furthermore, ventilation requirements (OR 20.187, $p<0.0001$), severe rises in SGOT (OR 5.387, $p<0.0001$) and SGPT levels (OR 5.538, $p<0.001$) upon admission were linked to a higher likelihood of the patient's death. We also did not find any connection between a patient's platelet deficiency and their risk of death but on other hand, patients displaying leucocytosis showed clear and statistically significant association with mortality ($p=0.001$). Moreover, our study did not reveal any relationship between severe complications of disease like encephalopathy/bleeding manifestations and likelihood of patient's death, although this finding needs further research.

There are limitations and strengths in our study. Study was conducted at single tertiary care facility, potentially limiting generalizability of findings to broader population. Study primarily focuses on SGOT and SGPT levels, potentially missing out on other relevant biomarkers that could provide more holistic understanding of paediatric dengue severity. Also, study's duration might not capture potential seasonal variations due to time constraints in dengue prevalence, affecting the generalizability of findings across different times of year.

Strengths of study showed that it employed both retrospective and prospective observational designs, providing comprehensive analysis of severe paediatric

dengue cases over an extended period. Rigorous scrutiny and validation processes employed during data collection, minimizing errors and ensuring data reliability. Study addresses critical need by investigating clinical variables associated with adverse outcomes in severe paediatric dengue and providing valuable insights into potential markers for assessing and predicting severity and mortality of severe dengue illness in paediatric patients.

CONCLUSION

The analysis revealed significant associations between various risk factors and clinical outcomes, highlighting the critical impact of factors such as PICU stay duration, ventilation requirement, and elevated liver enzyme levels on mortality. Logistic regression analysis further emphasized that substantial odds increase with prolonged PICU stay and ventilation requirements. Hence, the study provides valuable insights into the intricate relationship between these factors and dengue severity as well as clinical implications for risk stratification in the PICU setting, contributing to a more informed approach to managing severe dengue illness in children.

ACKNOWLEDGEMENTS

Authors would like to thank to Dr. V. V. Murthy and Dr. Latha M. S. for their invaluable contributions to the contrivance and formulation of this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Johnson DJ, Bandari B, Bachina P. A study of morbidity and mortality markers in children diagnosed with severe dengue illness at a quaternary paediatric intensive care unit. Int J Contemp Pediatr 2024;11:804-11.