

THE DAILY DENGUE SEVERITY SCORE ACCURACY IN THE ASSESSMENT OF SEVERE MANIFESTATIONS OF DENGUE INFECTION IN AGES 1 MONTH TO 18 YEARS OLD ADMITTED FROM 2018 TO 2020 IN PERPETUAL SUCCOUR HOSPITAL, IN CEBU CITY, PHILIPPINES



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BACKGROUND OF THE STUDY

- Dengue affects about 1% of the world's population annually and is associated with high morbidity.
- Cebu ranked the highest with 3,290 cases and 20 deaths (11.8% increased compared to the 3.267 cases with 16 death in 2018)²
- Several attempts were made to find a suitable marker to predict patients with Dengue who are at risk of subsequent severe manifestations of bleeding, plasma leakage, threatened shock and profound shock during the febrile and critical stages.
- · Scoring systems were formulated to evaluate or forecast disease severity based on epidemiological information and clinical signs or symptoms prior to laboratory results.
- The PELOD-2 Score³, Pediatric Risk of Mortality III-Acute Physiology Score (PRISM III-APS)4, pediatric Sequential Organ Failure (pSOFA)5 score, and the Pediatric Multiple Organ Dysfunction Score (P-MODS)⁶ in measuring the severity of multiple organ dysfunction in critically ill children admitted in the PICU are of the same importance.
- After several trials, the Daily Dengue Severity Score (DDSS) was formulated which has 14 parameters^{1.} A score of ≥12 accurately assesses severe manifestations. This scoring will be used in this study.

OBJECTIVES

General Objectives:

Determine the accuracy of the Daily Dengue Severity Score in the assessment of severe manifestations of patients ages 1 month to 18 years old admitted for Dengue Infection

Specific Objectives:

- To compare the clinicodemographic profile of the patients classified as Dengue without warning signs, Dengue with warning signs, and Severe Dengue
- To determine and compare the mean Daily Dengue Severity Score among patients classified as Dengue With warning signs, Dengue Without warning signs, and Severe Dengue
- To determine the sensitivity, specificity, positive likelihood ratio and overall accuracy of Daily Dengue Severity Score to predict Severe Dengue before defervescence phase.

METHODOLOGY

Study Design

Cross-Sectional Study

Study Population and Setting

- I month to 18 years old admitted from January 2018 to December 2020
- Laboratory confirmed Dengue Non-Structural Protein Antigen NS1 test or Dengue-specific lgM/lgG
- Exclusion criteria: admitted ≤ 24 hours in due to rapid deterioration leading to demise, transferred to another facility, or in recovery/defervescence phase

Sample Size and Sampling Procedure

$n = [Z2 \times P \times (1 - P)] / e2$

- Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)
- P = expected true proportion
- e = desired precision (half desired CI width)
- 327 case records which gualified out of 1,018 Dengue admissions
- Dengue without warning signs (N=34) Dengue with Warning Signs (N=271) Severe Dengue (N=22)
- The sample sizes for each year were then summed, in which a total a sample size of 327 was derived.
- Since the number of Severe Dengue comprised only 3% of the total Dengue cases, and Dengue Fever with Warning Signs comprised the largest percentage of 75%, a purposive sampling technique was applied with the objective of testing out the accuracy of the Daily Dengue Severity Score in the assessment of severe manifestations of Dengue.

Conceptual Framework



Daily Dengue Severity Score¹

- defervescence was designated as Day 0 (D0). One and 2 days before defervescence was
- designated as Day-1 (D-1) and Day-2 (D-2) and so on. One and 2 days after defervescence was designated as Day+1 (D+1) and Day+2 (D+2).

Data Analysis Tools

- Analysis of variance (ANOVA) Bonferonii
- Stata/SE 14.0 was used for the analyses (StataCorp. LP. Stata Statistical Software: Revised 2015. College Station, TX: StataCorp LP.)
- mean
- Area under the Receiver Operating Characteristic (AUROC) curves
- Sensitivity, Specificity, Positive likelihood ratio

RESULTS AND DISCUSSION

Mean Daily Dengue Severity Score



Increasing scores from D-2 and D-1 prior D0 in comparison to the succeeding days after D0 which showed decreasing geometric mean on D+1, D+2 and D+3

Positive Likelihood Ratio

Score- Classified Severity Level	Sensitivity (%)	Specificity (%)	Correctively Classified (%)	Positive Likelihood Ratio	
4	100.0%	22.2%	26.6	1.3	
5	100.0%	25.0%	29.21	1.3	
6	93.3%	35.3%	38.6	1.4	
7	93.3%	38.9%	41.95%	1.5	
8	80%	82.14%	82.02%	4.4	
9	73.33%	87.70%	86.89%	5.9	
10	66.67%	92.86%	91.39%	9.3	
11	46.6%	97.22%	94.38%	16.8	
12	40%	98.02%	94.76%	20.1	
13	40%	99.21%	95.88%	50.39	
15	33.33%	99.6%	95.88%	84.0	

 As the scores are increasing, there is also a higher likelihood of going into Severe Dengue, with cut points of 8, 9, and 10 had the ability to predict subsequent Severe Dengue at D-1

Distribution of Daily Dengue Severity Score at D-1



Relationship of the Classified Severity Level and Positive Likelihood Ratio

-Classified Severity level -Positive Likelihood Ratio

1 Tangnararatakit K, Chuansamit A, Watcharakakilok P, Apiwattanakal N, Lenthumian R, Keatika J, et al. Daily Dengue Severity Score to Assess Severe Manifestations. The Pediate 3. Department of Health. (Online).; 2019 [cited 2020 Aquat. Available from: HHVKLNN: "https://www.doh.gov.ph/press-release/DGH-DECLARES-NNTONN-DEMAGE-EPIDEMIC"

Clinicodemographic Profile

Patient Profiles	Diagnosis				
	Dengue without warning Signs (N=34)	Dengue with warning signs (N=271)	Severe Dengue (N=22)	P-valu	
Demographic					
Male, %	50.0	58.5	50.0	0.521	
Age (yr) (Mean ± SD) (month) (n=4)	9.2+5.0	8.2 ± 4.2	8.14±3.3	0.46	
Duration of fever (day) (Mean ± SD)	3.9±2.0*	4.2±1.5	5.1±3.5*	0.03	
Duration of hospitalization (day) (Mean # SD)	5.6±1.5*	5.8±2.7*	7.5 ± 2.4 **	0.008	
Hematological Status (Complete					
Blood Count)	41.2±4.2	39.6±4.8	40.5±5.0	0.16	
Initial Hematocrit (%)	42.2±4.5*	41.7±4.3*	46.3±6.0 **	0.000	
Highest Hematocrit	1.18.7±5.87	1.11.8±6.48	1.29.6±6.80	0.41	
Initial White Blood Cell	159.7±61.7	139.7±64.5	140.9±93.0	0.25	
count (103/ pL)	86.8±43.6 ⁴⁴	60.2±39.7 ^{b,c}	22.5 ± 21.1 ^{ab}	0.000	
Initial platelet count (×10 ³ /µL)					
Lowest platelet count (×10 ³ /µL)					
Bleeding sites (n.%)					
Epistaxis	2(5.9)	26(9.6)	1(4.6)	0.59	
Petechiae ± ecchymosis	7(20.6)	39(14.4)	9(40.9)	0.005	
Hypermenorrhea	0(0)	2(0.74)	0(0)		
Gross hematuria	0(0)	0(0)	0(0)	-	
Melena	0(0)	0(0)	0(0)		
Hematemesis	0(0)	0(0)	0(0)		
Hematochezia	0(0)	0(0)	0(0)		
Mode of presentation (n,%)					
Hepatomogaly	0(0)	20(7.4)	9(40.9)		
Headache	8(23.5)	41(15.1)	8(36.4)		
Myalgia	1(2.9)	24(8.9)	4(18.2)		
Vomiting	13(38.2)	118(43.5)	15(68.2)		
Cough	23(32.4)	219(19.2)	9(59.1)		
Abdominal pain	6(17.6)	100(36.9)	17(77.3)		
Hemodynamic status (Mean ±					
SD)	32.6± 5.1	33.8±6.2 ^b	29.5±8.4*	0.01	
Pulse pressure	98.8±9.1*	98.3±9.4 b	90.4±23.4**	0.005	
Systolic Blood Pressure	65.6±7.0	64.3±6.6	60.9±16.6	0.08	
Diastolic Blood Pressure			-		
Complications during admission					
Myocarditis	0.0 (0)	3(1.1)	4(18.2)		
Pleural effusion	0(0)	9(3.3)	14(63.6)		
Encephalitis	0(0)	0(0)	0(0)		
Presence of comorbidities (n,%)	1 (3.0)	2(0.7)	1(4.6)		
Discharged (n.%)	33(100.0)	271(100)	22(100)	0.05	

AUROC and Confidence Interval Analysis

	Dengue with	warning signs	Severe Dengue		
Days of illness	AUROC	95% CI	AUROC	95% CI	
D-4	0.66	0.42, 0.91	0.72	0.17, 1.0	
D-3	0.52	0.26, 0.79	0.92	0.77, 1.00	
D-2	0.54	0.39, 0.68	0.86	0.67, 1.00	
D-1	0.58	0.47, 0.68	0.89	0.80, 0.99	
D0	0.54	0.44, 0.644	0.73	0.59, 0.87	
D+1	0.53	0.42, 0.63	0.75	0.62, 0.88	
D+2	0.55	0.45, 0.66	0.68	0.54, 0.8	
D+3	0.63	0.52, 0.75	0.71	0.55, 0.87	

CONCLUSIONS

- . This scoring has the ability to assess subsequent severe manifestations leading to Severe Dengue at D-1 compared with other days.
- . The scores 8, 9, and 10 were the cut points to predict subsequent Severe Dengue at D-1.
- Sensitivity of 66.7% to 80%
- Specificity of 87.88% to 93.94% Positive likelihood ratio of 6.6 to 11
- Correctively classified patients of 85.42%

RECOMMENDATIONS

- . This scoring when adapted particularly in the Emergency Room, Pediatric Intensive Care Unit (PICU) or wards can help clinicians assess the possibility of progression to Severe Dengue.
- This scoring tool would also aid in the prompt management and timely referral before disease progression.
- The researcher recommends a continuation of this study be pursued prospectively with at least 3 scoring frequency every 8 hours within a 24-hour shift for more conclusive and reliable evidences.

4 Pelicisk MM, Fanni RM, Bastimano UE. The pediatric role of mortality IE— source phylology score (priorn IE-spc): A method of susoning phylologic instability for pediatric intensive care unit, patients: The Sustainal of Pediatrics: 1049-115(4):575-5 G-Mustainal GM, G-Melikawy MS, Zayan MK-Pediatric sequential region failure susonment (pld046) score: a new mortality prediction score in the pandatric intensive care unit. Anales de Pediatric (Ediatri), 2000;02(1):277-46.

geometric mean [mean±SD (geometric mean) and interquartile range (IQR)] of Dengue without warning signs showed 5.0±3.2 (5.2) IQR 5, Dengue with warning signs had 5.9±2.7 (5.4) IQR 2.5, and Severe Dengue had 12.1±5.2 (11.1), IQR 8.

- The mean, standard deviation, and



Mean Daily Dengue Severity Score using geometric

BACKGROUND

Dengue

 affects about 1% of the world's population annually and is associated with high morbidity

Daily Dengue Severity Score¹

- can help clinicians predict outcomes and provide timely management
- has 14 parameters related to clinical parameters and management with a score of
- Based on the pathophysiology of Dengue, the day of defervescence was designated as Day 0 (D0).
- One and 2 days before defervescence was designated as Day-1 (D-1) and Day-2 (D-2) and so on. One and 2 days after defervescence was designated as Day+1 (D+1) and Day+2 (D+2).

Cebu City

ranked the highest with 3,290 cases and 20 deaths (11.8% increased compared to the 3,267 cases with 16 death in 2018)²

Several Scoring Systems

- PELOD-2 Score³
- Pediatric Risk of Mortality III-Acute Physiology Score (PRISM III-APS)⁴
- pediatric Sequential Organ Failure (pSOFA) score⁵
- Pediatric Multiple Organ Dysfunction Score (P-MODS)⁶

OBJECTIVES

General Objectives

To determine the accuracy of the Daily Dengue Severity Score in the assessment of severe manifestations of Dengue Infection

Specific Objectives

- To compare the clinicodemographic profile of the patients classified as Dengue with or without warning signs, and Severe Dengue
- To determine and compare the mean Daily Dengue Severity Score among patients classified as Dengue with or without warning signs, and Severe Dengue
- To determine the sensitivity, specificity, positive likelihood ratio and overall accuracy of Daily Dengue Severity Score to predict Severe Dengue before defervescence phase

METHODOLOGY

Conceptual Framework CHILDREN (1 month - 18 years old) Dengue Infection: (+) Dengue NSI and/or (+) Dengue-Specific IgG/IgM **DENGUE FEVER DENGUE FEVER** WITH WARNING SIGN SEVERE DENGLI WITHOUT WARNING SIGNS Lives in or travel to dengue Abdominal pain or tenderness Severe plasma leakage Persistent vomiting Clinical fluid accumulation Severe hemorrhage endemic area, fever, and any 2 of the following criteria: Severe organ involvemen Mucosal bleed - Nausea and vomiting, Lethargy Rash, aches, and pains. Restlessness Tourniquet test positive, leukopenia, and any warning • Liver enlargment > 2 cm · Laboratory increase in hematocrit and sign. - Laboratory-confirmed concurrent with rapid decrease in platelet dengue count DAILY DENGUE SEVERITY SCORE VARIARIES (14) Co-morbid risk factors Maximum pulse rate for age Lowest systolic BP and pulse pressure Time to achieve pulse pressure of > 20mmHg & normal BP Amount of crystalloids Amount of colloids used Urine output Number of bleeding sites Amount of packed red blood cell Platelet concentrate transfused Number of major organ dysfunction Status of re-shock or requiring inotropic drug Requiring ventilator support Requiring invasive procedure Daily Dengue Severity Score ≥ 12 Severe Manifestations

Study Design

Cross-Sectional Study

Study Population and Setting

- 1 month to 18 years old admitted from January 2018 to December 2020
- Laboratory confirmed Dengue Non-Structural Protein Antigen NS1 test or Dengue-specific IgM/IgG
- Exclusion criteria: admitted ≤ 24 hours in due to rapid deterioration leading to demise, transferred to another facility, or in recovery/defervescence phase

METHODOLOGY

Sample Size

- n = [Z2 x P x (1 P)] / e2
- 327 case records which qualified out of 1,018 Dengue admissions

Data Analysis Tools

- Analysis of variance (ANOVA) Bonferonii
- Stata/SE 14.0 was used for the analyses (StataCorp. LP. Stata Statistical Software: Revised 2015. College Station, TX: StataCorp LP.)
- Mean Daily Dengue Severity Score using geometric mean
- Area under the Receiver Operating Characteristic (AUROC) curves
- Sensitivity, Specificity, Positive likelihood ratio

Sampling Procedure

- Purposive Sampling Technique
 - Dengue without warning signs (N=34) Dengue with Warning Signs (N=271) Severe Dengue (N=22)

Daily Dengue Severity Score



Mean Daily Dengue Severity Score



 Increasing scores from D-2 and D-1 prior D0 in comparison to the succeeding days after D0 which showed decreasing geometric mean on D+1, D+2 and D+3

Positive Likelihood Ratio



 As the scores are increasing, there is also a higher likelihood of going into Severe Dengue, with cut points of 8, 9, and 10 had the ability to predict subsequent Severe Dengue at D-1

Clinicodemographic Profile

Table A.1 Clinicodemographic Profiles of Patients						
Patient Profiles	Diagnosis					
	Dengue without warning Signs (N=34)	Dengue with warning signs (N=271)	Severe Dengue (N=22)	P-value		
Demographic Male, %	50.0	58.3	50.0	0.521		
Age (yr) (Mean \pm SD) (month) (n=4)	9.2±5.0	8.2 ± 4.2	8.14±3.3	0.46 -		
Duration of fever (day) (Mean \pm SD)	3.9±2.0ª	4.2±1.5	5.1±3.5ª	0.03		
Duration of hospitalization (day) (Mean \pm SD)	5.6± 1.5 ª	5.8± 2.7 ^b	$7.5\pm2.4^{a,b}$	0.008		
Hematological Status (Complete		2010 - 2010 - 1000	22	0.855.26		
Blood Count)	41.2±4.2	39.6±4.8	40.5±5.0	0.16		
Initial Hematocrit (%)	42.2±4.5 ^a	41.7±4.3 ^b	46.3±6.0 a,b	0.000		
Highest Hematocrit	1.18.7±5.87	$1.11.8 \pm 6.48$	1.29.6±6.80	0.41		
Initial White Blood Cell	159.7±61.7	139.7±64.5	140.9±93.0	0.25		
count ($10^3/\mu$ L)	86.8±43.6 ^{a,c}	60.2±39.7 ^{b,c}	22.5 ± 21.1 ^{a,b}	0.000		
Initial platelet count (×10 ³ /µL)						
Lowest platelet count $(\times 10^3/\mu L)$						
Bleeding sites (n,%)						
Epistaxis	2(5.9)	26(9.6)	1(4.6)	0.59		
Petechiae \pm ecchymosis	7(20.6)	39(14.4)	9(40.9)	0.005		
Hypermenorrhea	0(0)	2(0.74)	0(0)	-		
Gross hematuria	0(0)	0(0)	0(0)	-		
Melena	0(0)	0(0)	0(0)	-		
Hematemesis	0(0)	0(0)	0(0)	-		
Hematochezia	0(0)	0(0)	0(0)			
Mode of presentation (n,%)						
Hepatomegaly	0(0)	20(7.4)	9(40.9)			
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SD)	32.6± 5.1	33.8±6.2 ^b	29.5±8.4 ^b	0.01		
Pulse pressure	98.8±9.1ª	98.3±9.4 ^b	90.4±23.4 ^{a, b}	0.005		
Systolic Blood Pressure	65.6±7.0	64.3±6.6	60.9±16.6	0.08		
Diastolic Blood Pressure				0.0000		
Complications during admission						
Myocarditis	0.0 (0)	3(1.1)	4(18.2)			
Pleural effusion	0(0)	9(3.3)	14(63.6)			
Encephalitis	0(0)	0(0)	0(0)			
Presence of comorbidities (n.%)	1 (3.0)	2(0.7)	1(4.6)	- 1		
Discharged (n.%)	33(100.0)	271(100)	22(100)	0.05		
a,b,c statistical significance at p. val	ue <0.05	-(/				

Distribution of Dengue Severity Scores at D-1



 The mean, standard deviation, and geometric mean [mean±SD (geometric mean) and interquartile range (IQR)] of Dengue without warning signs showed 5.0±3.2 (5.2) IQR
 5, Dengue with warning signs had 5.9±2.7 (5.4) IQR 2.5, and Severe Dengue had 12.1±5.2 (11.1), IQR 8.

CONCLUSIONS

Daily Dengue Severity Score Accuracy in the Assessment of Severe Manifestations

- This scoring has the ability to assess subsequent severe manifestations leading to Severe Dengue at D-1 compared with other days
- The scores 8, 9, and 10 were the cut points to predict subsequent Severe Dengue at D-1

- Sensitivity of 66.7% to 80%
- Specificity of 87.88% to 93.94%
- Positive likelihood ratio of 6.6 to 11
- Correctively classified patients of 85.42%

Adaptation of the Daily Dengue Severity Scoring in the clinical practice

- This scoring when adapted particularly in the Emergency Room, Pediatric Intensive Care Unit (PICU) or wards can help clinicians assess the possibility of progression to Severe Dengue
- This scoring tool would also aid in the prompt management and timely referral before disease progression

Continuation Study

 The researcher recommends a continuation of this study be pursued prospectively with at least 3 scoring frequency every 8 hours within a 24-hour shift for more conclusive and reliable evidences