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Exploratory analysis of thromboelastogram changes following fluid resuscitation in dengue—preliminary insight for future research

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Abstract

***Objectives*: Dengue remains a serious global health concern, with substantial morbidity and mortality. However, there is a lack of objective evidence regarding the amount and type of fluid required for resuscitation, which is the cornerstone of dengue management. Thromboelastogram (TEG) parameters have been observed to be affected in dengue; however, there has been limited research investigating the real-time changes in TEG parameters related to fluid resuscitation. This study aimed to assess TEG changes after fluid resuscitation in dengue to enhance understanding of the pathophysiology and refine management strategies.**

***Design*: This was a prospective observational study with no intervention in the patient's diagnosis and management.**

***Setting*: Department of Emergency Medicine, Hospital Sungai Buloh, Malaysia.**

***Patients and participants*: 20 participants diagnosed with dengue underwent TEG assessment pre- and 1 hour after fluid resuscitation. Standardized clinical and laboratory data were collected, including vital signs, hematological parameters, coagulation profiles, and TEG parameters.**

***Results*: TEG parameters, specifically alpha angle and maximum amplitude, exhibited significant reductions post-resuscitation in dengue warning signs (p=0.019 and p=0.04). These findings suggest a potential link between fluid resuscitation and altered coagulation dynamics.**

***Conclusion*: This study offers insights into TEG changes post-fluid resuscitation, highlighting potential implications for glycocalyx disruption. Future research, including larger cohorts and exploration of different fluid types, is crucial for a comprehensive understanding of dengue pathophysiology and refining fluid resuscitation strategies.**

Keywords: Dengue, thromboelastogram, fluid resuscitation, endothelial glycocalyx disruption, platelet dysfunction.

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Introduction

Dengue fever, affecting over 390 million people annually across more than 100 countries, remains a formidable public health challenge, especially in endemic regions like Malaysia. (1,2) The incidence of dengue in Malaysia doubled between 2022 and 2023, with a persistently high fatality rate. (3,4)

The natural course of dengue fever encompasses three phases: febrile, critical/defervescence, and recovery stages. (5) The World Health Organization (WHO) reclassified dengue in 2009 to include warning signs that guide clinical management. Still, these classifications have been criticized for being based more on expert opinion than on clinical trial data. (6)

Managing severe dengue, particularly during the critical phase, requires careful fluid resuscitation to prevent shock while avoiding complications from fluid overload. Despite its central role in treatment, optimal fluid resuscitation strategies are not well-defined, as current guidelines are largely based on expert opinion rather than clinical evidence. (7,8)
Hematocrit level and serum lactate are often used as surrogate indicators of fluid resuscitation adequacy, although they do not directly reflect the impact of fluid on dengue pathophysiology. (6,7)
Thromboelastography (TEG) and rotational thromboelastometry (ROTEM) have emerged as rapid, bedside coagulation assays that provide real-time insights into clot formation kinetics and platelet function. (8,9) TEG assesses the global viscoelastic properties of whole blood, providing specific parameters that delineate various stages of hemostasis. These parameters include the reaction time (R time), indicating the duration from test initiation to initial fibrin formation; the alpha angle, reflecting the rapidity of fibrin generation; maximum amplitude (MA), signifying clot strength and stability; the percentage of clot lysis after 30 minutes (LY30), quantifying fibrinolysis extent post-MA; and the coagulation index, the parameter defining overall coagulation status.
TEG provides valuable insights into coagulation dynamics and has shown alterations in dengue patients, particularly reductions in MA, indicating possible platelet dysfunction. (9,10) However, the impact of fluid resuscitation on TEG parameters remains underexplored, presenting a gap in the understanding of dengue management.
This study aimed to explore the effects of fluid resuscitation on TEG parameters in dengue patients. As an exploratory analysis, it sought to generate hypotheses and identify trends for future research, contributing to the development of evidence-based guidelines.

Methodology

Study design

This prospective observational study investigated changes in TEG parameters following fluid resuscitation in patients diagnosed with dengue fever. The study design was exploratory, focusing on identifying trends that could inform larger, more definitive studies in the future.

Participants

Twenty participants with confirmed dengue fever, as evidenced by positive non-structural protein-1 (NS1) or immunoglobulin M (IgM) tests, were recruited from the Emergency Department of Hospital Sungai Buloh, a tertiary care center. Inclusion criteria included serologically confirmed dengue fever with no prior fluid resuscitation or less than 250 ml of crystalloid administered before enrollment. Exclusion criteria were pre-existing coagulation disorders, recent steroid use, and active bleeding.
Patients were categorized according to WHO criteria as having either severe dengue or dengue with warning signs. Severe dengue was defined by the presence of severe plasma leakage, bleeding, or organ involvement, while warning signs included symptoms such as abdominal pain, persistent vomiting, and rapid platelet drop.

Fluid resuscitation protocol

Fluid resuscitation was administered according to standard clinical guidelines for dengue management, with adjustments made by the clinical team based on individual patient needs. Patients with severe dengue received normal saline at 10 ml/kg/hour, while those with warning signs received 5–7.5 ml/kg/hour. The research team did not intervene in clinical management.

Thromboelastogram analysis

TEG assessments were conducted using the TEGR 5000 hemostasis machine, with personnel trained to ensure optimal results. The parameters evaluated included reaction time (R time), alpha angle, MA, LY30, and the coagulation index. Measurements were taken at baseline (pre-fluid resuscitation) and one hour post-resuscitation to capture changes in coagulation dynamics.

Ethical considerations

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Research Management and Ethical Committee of the Ministry of Health Malaysia (NMRR-17-28-33855), and informed consent was obtained from all participants or their legally authorized representatives.

Statistical analysis

Data were analyzed using SPSS Version 24. Descriptive statistics, including means, standard deviations, and interquartile ranges, were used to summarize demographic, clinical, and laboratory data. The Wilcoxon signed-rank test was used to assess changes in TEG parameters pre- and post-fluid resuscitation. Given the exploratory nature of the study, formal sample size calculations were not performed.

Sample size justification

The absence of prior research on TEG changes post-

fluid resuscitation in dengue necessitated an exploratory approach, with a small sample size chosen to identify trends and generate hypotheses. These preliminary results will inform the design of future studies with larger, more precisely determined sample sizes.

Results

The study population consisted of 20 patients: 12 with dengue warning signs and 8 with severe dengue. The mean age was 26.2 years (±4.82) in the warning signs group and 33.6 years (±10.68) in the severe dengue group. The majority of patients were Malay, with a small representation of Chinese and Indian patients. The distribution by race and comorbidities is summarized in **Table 1**.

Clinical parameters pre- and post-fluid resuscitation

Table 2 outlines the vital signs of patients pre- and post-fluid resuscitation. Significant reductions in pulse rate (p=0.017) were observed in the warning signs group. In contrast, the severe dengue group showed non-significant trends in post-resuscitation changes in mean arterial pressure and respiratory rate.

Laboratory parameters pre- and post-fluid resuscitation

Table 3 presents laboratory parameters before and after fluid resuscitation. Notable changes were observed in hemoglobin levels (p=0.014) and lactate levels (p=0.021) in the warning signs group. In the severe dengue group, significant changes were seen in hemoglobin levels (p=0.008) and activated partial thromboplastin time (aPTT) (p=0.045).

TEG parameters pre- and post-fluid resuscitation

TEG parameters pre- and post-fluid resuscitation are depicted in **Table 4**. Significant reductions in alpha angle (p=0.019) and MA (p=0.04) were noted in the warning signs group post-resuscitation. Although reductions were also observed in the severe dengue group, these did not reach statistical significance.

Discussion

This exploratory study provides important preliminary insights into the effects of fluid resuscitation on thromboelastogram parameters in dengue patients, with particular focus on alpha angle and MA. The significant reductions in these parameters observed post-resuscitation, especially in the warning signs group, suggest that fluid resuscitation may impact coagulation dynamics, potentially through mechanisms involving endothelial glycocalyx disruption. The glycocalyx is a critical structure that maintains vascular integrity and regulates coagulation; its disruption could lead to increased vascular permeability, inflammation, and coagulopathy, all of which are relevant in the pathophysiology of severe dengue.

One of the central findings of this study is the potential link between fluid resuscitation and altered coagulation dynamics, as indicated by the changes in TEG parameters. This aligns with prior research suggesting that large fluid volumes can exacerbate glycocalyx degradation, leading to complications such as capillary leakage and platelet dysfunction. (11–13) These results underscore the need to carefully consider fluid type and volume in dengue management to avoid adverse outcomes.

These findings have important implications for clinical practice. They suggest that current fluid resuscitation protocols for dengue may need to be re-evaluated, particularly in the context of balancing the benefits of volume expansion against the risks of disrupting coagulation dynamics. While the study's small sample size limits the ability to draw definitive conclusions, the consistency of the trends observed highlights the potential need for more individualized fluid management strategies in dengue, possibly incorporating real-time TEG monitoring to guide resuscitation.

The main limitation of this study was its small sample size, which limited the generalizability of the findings. The primary reason for this limitation was the substantial financial cost associated with conducting TEG assessments. Each TEG test is expensive, and the cost of analyzing the 20 samples in this study was approximately RM 50,000. This financial constraint prevented the inclusion of a larger cohort, which would have provided greater statistical power. It allowed for a more comprehensive analysis of the effects of fluid resuscitation on coagulation in dengue patients.

Despite the limited sample size, the consistent trends observed across the cohort are noteworthy. These findings highlight the potential importance of coagulation monitoring in dengue management and suggest avenues for future research. Larger studies with adequate funding are needed to confirm these preliminary findings and explore the underlying mechanisms in greater depth. Comparative studies that investigate different types of fluids and their impact on TEG parameters, as well as the volume and timing of fluid administration, will be particularly valuable.

Furthermore, future research should include more diverse patient populations and longitudinal designs

that track TEG changes at multiple time points post-resuscitation. This would provide a more detailed understanding of the temporal dynamics of coagulation in response to fluid therapy and help refine resuscitation strategies to improve patient outcomes in severe dengue.

In conclusion, this study offers valuable early insights into the impact of fluid resuscitation on TEG parameters in dengue patients. While the findings are preliminary and limited by the small sample size, they provide a foundation for future research aimed at optimizing fluid resuscitation strategies in dengue. Addressing the financial constraints that limit sample size in such studies will be crucial for advancing our understanding of dengue pathophysiology and improving clinical practice.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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Table 1. Demographic characteristics of patients

	Warning signs (n=12)	Severe dengue(n=8)
Age (years), mean±SD	26.2±4.82	33.6±10.68
Race, n (%) - Malay - Chinese - Indian	 10 (83.3%) 1 (8.3%) 1 (8.3%)	 5 (62.5%) 1 (12.5%) 1 (12.5%)
Co-morbidity, n (%) - hypertension - Dyslipidaemia - No known medical illness	 0 0 12 (100%)	 2 (25%) 1 (12.5%) 5 (62.5%)
Amount of fluid transfusion in 1 hour (ml), mean±SD	261.9±133.42	608.3±115.3
Length of hospital stay (days), median (Q1-Q3)	4.0 (3.0–4.8)	4.0 (2.0–8.0)
Length of ICU stay (days), median (Q1-Q3)	0 (0–0)	0.5 (0–4.5)
NS1 positive, n (%) - No - Yes	 0 12 (100%)	 1 (12.5%) 7 (87.5%)
IgG positive, n (%) - No - Yes	 9 (75%) 3 (25%)	 7 (87.5%) 1 (12.5%)
IgM positive, n (%) - No - Yes	 9 (78.6%) 3 (21.4%)	 8 (100%) 0 (0%)

Legend: SD=standard deviation; ICU=intensive care unit; NS1=non-structural protein-1; IgG=immunoglobulin G; IgM=immunoglobulin M.

Table 2. Vital signs of patients pre- and post-fluid resuscitation

	Warning signs (n=12)			Severe dengue (n=8)		
	Pre	Post	p-value*	Pre	Post	p-value*
	Median (Q1-Q3)	Median (Q1-Q3)		Median (Q1-Q3)	Median (Q1-Q3)	
MAP (mmHg)	90.0 (80.3–99.0)	89.0 (80.5–94.0)	0.833	80.0 (67.8–96.8)	95.0 (69.0–104.0)	0.236
Pulse rate (/min)	94.5 (85.0–107.5)	85.5 (75.5–98.5)	0.017	96.5 (82.0–109.8)	91.0 (80.8–98.8)	0.307
Respiratory rate (/min)	18.5 (18.0–19.8)	19.0 (18.0–20.0)	0.180	19.5 (18.0–20.0)	18.0 (16.0–18.0)	0.039
SpO2 (%)	100.0 (99.0–100.0)	99.0 (98.3–99.0)	0.121	98.5 (97.3–100.0)	98.5 (98.0–100.0)	0.157

Legend: Q1=quartile 1; Q3=quartile 3; MAP=mean arterial pressure; SpO2=peripheral oxygen saturation.
*Wilcoxon signed rank test.

Table 3. The laboratory parameters pre- and post-fluid resuscitation

	Warning signs (n=12)			Severe dengue (n=8)		
	Pre	Post	p-value*	Pre	Post	p-value*
	Median (Q1-Q3)	Median (Q1-Q3)		Median (Q1-Q3)	Median (Q1-Q3)	
WCC (×10⁹/l)	3.5 (2.0–4.8)	3.0 (2.0–4.0)	0.257	4.0 (3.0–6.5)	3.5 (2.3–6.0)	0.157
Haematocrit (%)	48.0 (42.3–50.8)	44.5 (41.5–48.5)	0.108	44.0 (39.3–49.8)	39.5 (37.0–45.0)	0.017
Haemoglobin (g/dl)	17.0 (14.3–17.8)	15.5 (14.3–16.8)	0.014	15.0 (13.3–16.8)	13.5 (12.3–15.0)	0.008
Platelet (×10⁹/l)	86.0 (43.0–171.3)	60.0 (34.3–122.5)	0.013	70.5 (15.8–150.8)	62.5 (15.5–130.8)	0.116
PT (seconds)	12.0 (12.0–12.0)	12.0 (12.0–13.0)	>0.995	13.0 (11.3–13.0)	13.0 (11.0–14.0)	>0.995
aPTT (seconds)	40.0 (38.0–47.0)	37.0 (34.5–48.5)	0.045	40.5 (34.0–45.8)	42.0 (32.0–46.0)	0.059
INR	1.0 (1.0–1.0)	1.0 (1.0–1.0)	>0.995	1.0 (1.0–1.0)	1.0 (1.0–1.0)	>0.995
Fibrinogen (mg/dl)	311.0 (277.0–362.5)	385.5 (248.0–2664.3)	0.109	350.0 (284.0–467.0)	[#]	0.18
Lactate (mmol/l)	2.0 (1.3–2.0)	1.0 (1.0–1.8)	0.021	3.0 (2.0–4.5)	2.0 (1.0–3.8)	0.023
Bicarbonate (mmol/l)	24.0 (24.0–26.0)	25.0 (23.3–26.0)	0.861	23.5 (21.3–26.3)	23.0 (22.0–27.0)	0.257
Base excess (mmol/l)	1.0 (0.0–3.5)	1.5 (0.0–4.0)	0.524	-1.0 (-1.8–2.3)	-0.5 (-2.0–2.8)	0.854
pH	7.42 (7.40–7.46)	7.40 (7.37–7.43)	0.655	7.44 (7.39–7.46)	7.42 (7.39–7.46)	0.317

Legend: Q1=quartile 1; Q3=quartile 3; WCC=white blood cell count; PT=prothrombin time; aPTT=activated partial thromboplastin time; INR=international normalised ratio.
*Wilcoxon signed-rank test. [#]Fibrinogen measurements were available for only 2 of 8 patients; therefore, summary statistics were not calculated.

Table 4. TEG parameters pre- and post-fluid resuscitation

TEG parameters	Normal value	Warning signs (n=12)			Severe dengue (n=8)		
		Pre	Post	p-value	Pre	Post	p-value
		Median (Q1-Q3)	Median (Q1-Q3)		Median (Q1-Q3)	Median (Q1-Q3)	
R time	5–10 min	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.636	0.5 (0.4–0.7)	0.4 (0.3–0.5)	0.361
K time	1–3 min	2.5 (2.0–5.0)	3.5 (2.0–5.0)	0.558	3.0 (1.0–6.0)	4.0 (2.0–6.0)	0.257
Alpha angle	53–72 deg	68.5 (61.8–73.8)	64.5 (60.8–71.8)	0.019	69.0 (66.5–73.3)	69.5 (66.5–72.3)	0.863
MA	50–70 mm	47.0 (37.0–56.0)	41.5 (36.0–52.8)	0.040	41.0 (28.5–56.8)	38.0 (28.0–53.0)	0.136
LY30	0–8%	0.0 (0.0–0.8)	0.0 (0.0–1.5)	0.655	0.0 (0.0–1.0)	0.0 (0.0–2.0)	0.564

Legend: TEG=thromboelastography; Q1=quartile 1; Q3=quartile 3; R time=reaction time; MA=maximum amplitude; LY30=percent lysis at 30 minutes.

References

1. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. Nature. 2013;496(7446):504–7.
2. AbuBakar S, Puteh SEW, Kastner R, Oliver L, Lim SH, Hanley R, et al. Epidemiology (2012-2019) and costs (2009-2019) of dengue in Malaysia: a systematic literature review. Int J Infect Dis 2022;124:240–7.
3. Khaw WF, Razali MF, Shamsuddin N, Zainal Abidin NF, Chan YM. Ten-year mortality study of dengue in Malaysia. IJID Reg. 2024;13:100455.
4. Malaysia: Dengue Outbreak - Nov 2023 [Internet]. 2023 Nov 17 [cited 2024 Jan 4]. Available from: https://reliefweb.int/disaster/ep-2023-000221-mys
5. Kamaruzaman H. CPG Management of Dengue Infection in Adults (3rd Edition) [Internet]. Putrajaya, Malaysia: Ministry of Health Malaysia; 2015 [cited 2025 Jun]. Available from: https://www.researchgate.net/publication/321936837_CPG_Management_of_Dengue_Infection_in_Adults_3rd_Edition
6. Alexander N, Balmaseda A, Coelho ICB, Dimaano E, Hien TT, Hung NT, et al. Multicentre prospective study on dengue classification in four South-east Asian and three Latin American countries. Trop Med Int Health 2011;16:936–48.
7. Madanayake P, Jayawardena A, Wijekoon SL, Perera N, Wanigasuriya J. Fluid requirement in adult dengue haemorrhagic fever patients during the critical phase of the illness: an observational study. BMC Infect Dis 2021;21:286.
8. Borré-Naranjo D, Cárdenas-Bolívar Y, Manzur-Barbur MC, Toro E, Buendia E, Martínez MC, et al. Fluid Management in Dengue Critical Phase: Which, When, How Much? Int Arch Med Microbiol 2022;4:015.
9. Sureshkumar VK, Vijayan D, Kunhu S, Mohamed Z, Thomas S, Raman M. Thromboelastographic analysis of hemostatic abnormalities in dengue patients admitted in a multidisciplinary intensive care unit: A cross-sectional study. Indian J Crit Care Med 2018;22:238–42.
10. Syed Abas SS, Abdul Karim N, Periyasamy P, Yusof N, Shah SA, Leong TT, et al. Correlation of Dengue Warning Signs during Febrile Phase with Rotational Thromboelastometry, Cortisol and Feritin. Int J Environ Res Public Health 2022;19:807.
11. Srikiatkhachorn A, Kelley JF. Endothelial cells in dengue hemorrhagic fever. Antiviral Res 2014;109:160–70.
12. Hippensteel JA, Uchimido R, Tyler PD, Burke RC, Han X, Zhang F, et al. Intravenous fluid resuscitation is associated with septic endothelial glycocalyx degradation. Crit Care 2019;23:259.
13. Byrne L, Obonyo NG, Diab SD, Dunster KR, Passmore MR, Boon AC, et al. Unintended consequences: Fluid resuscitation worsens shock in an ovine model of endotoxemia. Am J Respir Crit Care Med 2018;198:1043–54.