

Clinical Predictors of Severe Dengue

Qurrat-Ul-Ain Usmani¹, Jameel Muqtadir¹, Yousra Arshad¹, Hudaubiya Ayub¹

¹Department of Internal Medicine, Ziauddin University Hospital, Karachi, Pakistan

ABSTRACT

Background: Dengue fever is a significant public health concern, with severe cases leading to life-threatening complications. Early identification of severe dengue can improve patient outcomes and optimize healthcare resource utilization. The objective of the study was to evaluate clinical and laboratory predictors of severe dengue and their utility in clinical decision-making.

Methods: A prospective cohort study was conducted at Ziauddin Hospital, Karachi, from February to September 2024. A sample size of 66 with a 95% confidence interval and 5% level of significance was calculated using OpenEpi. The convenience sampling technique was used. Patients were categorized into two groups: Group A (≥ 3 warning signs or comorbidities) and Group B (≤ 3 warning signs, no comorbidities). Data were collected using a structured proforma and analyzed in SPSS 25. Logistic regression and receiver operating characteristic analysis were used to evaluate different predictors of severe dengue. Receiver operating characteristic analysis was used to evaluate different predictors of severe dengue. A p-value of less than 0.05 was considered significant.

Results: The mean age was 35.93 ± 14.96 years, with 66.7% males. Significant predictors included a fall in pulse pressure ($p=0.002$), elevated AST levels ($p=0.04$), AST/platelet ratio (APR) ($p=0.003$), and hypoalbuminemia ($p<0.0001$). The predictive model, including APR and fall in pulse pressure ($\chi^2 = 4.651$, $p=0.702$), explained 68.5% of severe dengue variance and had excellent discriminatory power (AUC=0.961) with 100% sensitivity and 91.1% specificity.

Conclusion: Clinical parameters such as pulse pressure and APR are reliable predictors of severe dengue. Further validation in larger cohorts can refine risk stratification and enhance management strategies.

Keywords: Dengue, Dengue Hemorrhagic Fever, Platelet Count, AST, Serum Albumin.

Corresponding Author:

Dr. Qurrat-Ul-Ain Usmani,

Department of Internal Medicine,
Ziauddin University Hospital,
Karachi, Pakistan.

Email: q.usmani@gmail.com

ORCID: <https://orcid.org/0009-0004-9994-3988>

Doi: <https://doi.org/10.36283/ziun-pjmd14-2/045>

How to cite: Usmani QUA, Muqtadir J, Arshad Y, Ayub H Clinical Predictors of Severe Dengue. Pak J Med Dent. 2025 April ;14(2): 294-300. Doi: <https://doi.org/10.36283/ziun-pjmd14-2/045>.

Received: Wed, October 9, 2024 **Accepted:** Wed, March 26, 2025 **Published:** Sun, April 13, 2025

INTRODUCTION

Dengue fever has been declared one of the "top ten threats to global health in 2019" by the World Health Organization¹. A high number of cases occur in the rainy season in the Subcontinent². The disease has now spread to less tropical and more temperate countries such as Nepal, which traditionally never saw the disease³. Pakistan has seen a rise in dengue fever cases and deaths over the last many years⁴.

Most of the individuals infected with the dengue virus have either a subclinical infection or fever and myalgia syndrome⁵. A small proportion of these patients enter a critical phase as fever declines and plasma leakage occurs, leading to severe dengue⁶. Shock, respiratory distress, bleeding, and organ dysfunction occur in a fraction of these, depending upon certain host and viral factors⁷. Heterotypic reinfection can result in classic dengue without/with warning signs or severe dengue as a result of antibody-dependent enhancement⁸.

The infection is characterized by an acute phase lasting for 3-6 days, which is followed by a short-lived critical phase during which defervescence and plasma leak occur until the recovery phase ensues⁹. Viral detection is usually done using the NS1 antigen¹⁰. Various other clinical and laboratory markers are used for monitoring disease progression¹¹. Dengue Score predicts the development of vascular leaks using serum albumin, hematocrit, platelets, and AST ratio¹².

During dengue epidemics, predicting severe dengue remained a significant challenge for clinicians, particularly when optimal resource allocation was crucial¹³. Identifying patients at risk of severe disease helped guide timely interventions and ensured that intensive care was reserved for those who truly needed it¹⁴. This study aimed to evaluate the predictive value of the Dengue Score alongside various clinical and laboratory markers within the healthcare system. By assessing their applicability, it sought to determine whether escalating care to the intensive care unit was always justified. The objective of this study was to analyze the effectiveness of these predictive models in optimizing resource utilization and improving patient outcomes.

METHODS

The study was conducted as a prospective cohort study in all three campuses of Ziauddin Hospital Karachi from February 2024 to September 2024. Permission was obtained from the hospital ethical review committee prior to the commencement of the study (ERC Number: 8540324QUMED). A thorough written informed consent was also obtained from the patients prior to inclusion in the study. Patients were informed in detail regarding the

collection of their data at the time of enrollment. The sample size was calculated by using the OpenEpi sample size calculator by using a previous study done on Clinical Profile and predictors of Severe Dengue Disease in South India¹⁵. In this study, the authors found that the prevalence of elevated hematocrit in severe dengue patients was 64.9% and 28.1% in non-severe dengue patients. The confidence level was kept at 95%, and the power of the study was at 80%. The calculated sample size came out to be 66. Sampling was done via a convenience sampling technique. All patients of dengue fever being admitted to the wards were included if they met the criteria. The patients were divided into two groups of 33 patients each. Both groups included patients of dengue fever with warning signs admitted to the Medical Inpatient department (High Dependency Unit or Medical Ward).

Group A included patients with >3 warning signs as defined by the WHO Dengue Severity Classification or a co-existing comorbidity such as diabetes, hypertension, ischemic heart disease, and chronic kidney disease. Group B included patients who had ≤ 3 of the warning signs and no comorbidities¹³. Patients of age above 15 years, either gender, diagnosed with dengue fever by NS-1 or Dengue IgM positivity, presenting before 5th day of illness and admitted to the medical unit were enrolled in the study, while patients who refused to participate in the study, presented beyond 5th day of illness, had organ failure or dengue shock at the time of presentation or concurrently having another infectious disease were excluded from the study. The enrolled patients were followed for 72 hours starting from enrollment to stepping up to ICU until their platelet count began to rise or they were stepped down to ward-based care or discharged. Data collection was done using a specialized proforma filled by the researcher herself.

The collected data were entered into the Statistical Package for Social Sciences software v. 25. Percentages and frequencies were calculated for qualitative variables such as gender, comorbid conditions, symptoms, signs, thrombocytopenia, dengue score, and development of severe dengue and ICU admission. Mean and standard deviation were calculated for quantitative data such as age, hematocrit, ALT, platelet count, serum albumin, and pulse pressure. Comparison was made between the variables for both groups using an independent samples t-test for quantitative variables, and a Pearson Chi square test was done for categorical variables. A p-value of less than 0.05 was considered significant. Logistic regression analysis was used to highlight the relationship between several clinical/laboratory parameters and Dengue Score and progression to severe dengue.

RESULTS

Table 1: Characteristics of Group A Versus Group B

Characteristics		Group A	Group B	p-value
		(n=33)	(n=33)	
Age		34.09±13.90	37.78±15.95	0.319
Gender	Male	21(63.64%)	23(69.7%)	0.794
	Female	12(36.36%)	10(30.3%)	
Day of Illness	5 th	0	7(21.21%)	0.056
	6 th	10(30.3%)	6(18.18%)	
	7 th	6(18.18%)	8(24.24%)	
	8 th	12(36.36%)	9(27.27%)	
	9 th	5(15.15%)	3(9.09%)	
Comorbidities	Diabetes	6(18.18%)	12(36.36%)	0.097
	Hypertension	3(9.09%)	6(18.18%)	0.282
	CKD	0	4(12.12%)	0.039
	Ischemic Heart Disease	1(3.03%)	3(9.09%)	0.302
	Combinations	1(3.03%)	8(24.24%)	-
Symptoms	Abdominal Pain	33(100%)	22(66.67%)	<0.0001
	Persistent Vomiting	33(100%)	19(57.58%)	<0.0001
	Early Rash	18(54.55%)	14(42.42%)	0.325
	Late Rash	23(69.7%)	5(15.15%)	<0.0001
	Hemorrhagic Complications	28(84.85%)	7(21.21%)	<0.0001
Clinical Signs	Lowest Pulse Pressure	31.54±6.06	32.51±7.65	0.57
	Fall in Pulse Pressure	13.72±8.16	11.36±7.72	0.232
Laboratory Values	Highest recorded Hematocrit?	43.21±8.97	41.21±6.38	0.301
	Rise in the Hematocrit	4.15±2.9	5.15±3.2	0.213
	Lowest recorded Platelet count	52.30±51.91	41.42±38	0.335
	Lowest recorded TLC	3.2±0.99	4.26±1.57	0.003
	Highest AST levels (IU/L)	239±377.92	78.30±26.15	0.017
	AST ratio	4.27±6.74	1.39±0.46	0.017
	Lowest Serum Albumin (mg/dL)	3.25±0.51	3.55±0.5	0.02
	AST / Platelet ratio	19.43±33.27	5.46±6.13	0.021
	Acute Kidney Injury	2(6.06%)	4(12.12%)	0.392

A total of 66 patients with dengue fever were enrolled and divided into two groups, **A** and **B**, in a 1:1 ratio, based upon the number of warning signs delineated by the WHO-2009 criteria. The mean age of patients was 35.93±14.96 years. There were 66.7% (n=44) males and 33.3% (n=22) females in the sample. A total of 28 patients had some underlying chronic illness. The symptomatology, clinical, and laboratory parameters of Groups A and B have been summarized in **Table 1**.

When Groups A and B were compared against whether patients developed severe dengue or not as per WHO-20009 criteria, no significant difference was observed ($p=0.6330$). Similarly, the relationship between ITC admission and groups A and B was not found to be significant ($p=0.391$). However, almost all of the patients who later went on to develop severe dengue as per WHO 2009 criteria were shifted to ITC by their healthcare team ($p<0.0001$). While comparing the dengue score against the ITC admission, it was found that higher scores were likely to be shifted to ITC as opposed to lower scores and were more likely to go on and develop severe dengue ($p=0.001$, $p<0.0001$). Low platelet count was the most significant cause of ITC admission ($p<0.0001$).

Table 2: Logistic Regression and ROC Analysis for Dengue Score

Variable	Coefficient B	p-value	OR	95% CI
Dengue Score (1 – 4)	2.304	0.003	10.011	2.161 – 46.387
Constant	-5.95	<0.0001	0.003	-
-2 LL Ratio	40.064			
Cox & Snell R ²	0.216			
Nagelkerke R ²	0.377			
Hosmer-Lemeshow χ^2 (p-value)	7.454 (0.024)			
ROC Curve AUC (95% CI)	0.808 (0.645 – 0.971)			

Logistic regression performed for the Dengue score showed that it is a reliable predictor of severe dengue ($B=2.304$, $OR=10.011$, $p=0.003$), indicating higher scores were strongly associated with severe dengue. Dengue Score had a moderate explanatory power (Cox & Snell $R^2=0.216$, Nagelkerke $R^2=0.377$), and it was not a perfect fit ($\chi^2=7.54$, $p=0.024$). However, an AUC of 0.808 was identified in the ROC curve with an optimal cut-off corresponding to a score midway between 1 and 2, having a sensitivity of 80% and a specificity of 55.4% (Table 2).

Table 3: Logistic Regression and AUC for Various Parameters

Variable	Coefficient B	Odds Ratio	p-value	AUC
Lowest Pulse Pressure	-0.39	0.677	<0.0001	0.065
Pulse Pressure Fall	0.354	1.424	0.002	0.949
Rise in the Hematocrit	-0.017	0.983	0.874	0.546
Highest Hematocrit	-0.093	0.911	0.072	0.661
Lowest Platelet Count	0.016	1.016	0.179	0.345
Lowest TLC	-0.079	0.924	0.743	0.586
Highest AST levels (IU/L)	-0.007	0.993	0.04	0.762
AST ratio	-0.401	0.67	0.04	0.762
1 / Serum Albumin (mg/dL)	-35.849	<0.0001	<0.0001	0.889
AST / Platelet ratio	-0.056	0.945	0.003	0.764

Univariate logistic regression analysis performed for other variables identified some other significant predictors besides variables of Dengue score, of the outcome as well, like fall in pulse pressure ($p=0.001$) and AST to platelet ratio (0.003).

Based on this logistic regression, only AST to Platelet ratio and fall in pulse pressure were combined in a model that performed even better than Dengue Score for predicting severe Dengue with a sensitivity of 100% and a specificity of 91.1. The better performance of the Dengue Score is attributable to it being a single score, whereas this model has two variables. If these variables were to be combined as a single score, they could outperform the dengue score (Table 3).

Table 4: Summary of Our Model

Variable	Coefficient B	p-value	OR	95% CI
AST: Plt count	0.028	0.097	1.028	0.995 – 1.063
Fall in Pulse Pressure	0.308	0.012	1.36	1.069 – 1.731
Constant	-8.048	0.898	1.121	-
-2 LL Ratio	23.277			
Cox & Snell R ²	0.392			
Nagelkerke R ²	0.685			
Hosmer-Lemeshow χ^2 (p-value)	4.651 (0.702)			
ROC Curve AUC (95% CI)	0.961 (0.971 – 1.00)			

While the Dengue Score had a strong association with severe dengue (OR = 10.011, p = 0.003), its model fit was weaker, with lower predictive power (Nagelkerke R² = 0.377) and poor calibration (Hosmer-Lemeshow p = 0.024). In contrast, our model, which just included fall in pulse pressure and AST to platelet ratio, was a better fit (-2LL = 23.277), had higher predictive power (Nagelkerke R² = 0.685), and excellent discrimination (AUC = 0.961). A fall in pulse pressure was a significant predictor (OR = 1.36, p = 0.012), but AST to platelet ratio had a weaker effect (OR = 1.028, p = 0.097). Overall, our model was more reliable and clinically useful in identifying severe dengue cases (Table 4, Figure 1).

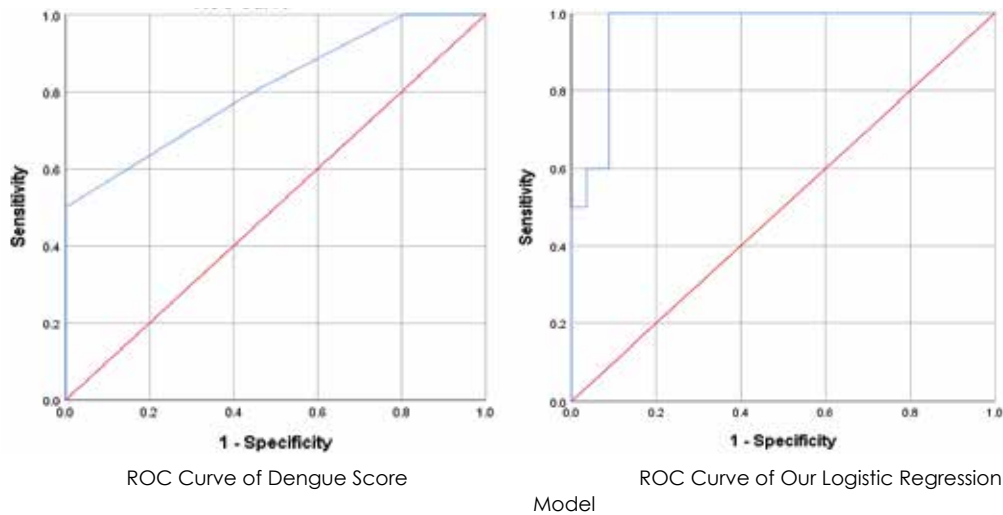


Figure 1: ROC Curve of Dengue Score versus Our Model

DISCUSSION

Dengue score exhibited a reasonable sensitivity but low specificity, limiting its utility as a standalone predictor for severe dengue. A constraint was the small sample size, which restricts the generalizability of findings to broader populations. However, with a high sensitivity, the Dengue score is still a valuable tool in clinical settings⁹. However, there is a need for a more robust and comprehensive risk stratification

approach.

Clinical and laboratory parameters varied between groups. Logistic regression analysis revealed that several parameters, including fall in pulse pressure, serum albumin levels, AST levels, AST/platelet ratio, and AST ratio, were significant predictors of severe dengue. The final model, made by the authors by adopting a more clinical and easy approach,

consisted of only the AST to platelet ratio and a fall in pulse pressure. This was able to predict 68.5% variability in the data and had excellent discriminatory power. Omitting the routine use of serum albumin can decrease the number of laboratory tests and cut costs. However, a single region's data limits this study's ability to capture variations in disease presentation and outcomes across different healthcare settings. The inclusion of additional machine learning techniques or validation cohorts could strengthen the predictive models' reliability and performance metrics.

It has been suggested in a study done in Saudi Arabia over four years that the World Health Organization's dengue classification scheme had low sensitivity for identifying patients in need of advanced health care¹⁶. Also, there is a need to account for chronic illnesses, which might get decompensated¹⁷. A study in Sri Lanka on 388 patients identified that it has a higher sensitivity but a lower specificity compared to the physicians' gestalt. This is again a stressor upon the fact that clinical judgement is of paramount importance while dealing with these patients, even though several classification and predictive models exist¹⁸. A study done in Thailand used six parameters, including serum albumin, AST, ALT, platelet count, partial thromboplastin time, and dengue IgM, for creating a score to predict dengue. Their model had an AUC in the ROC analysis of 0.902, a sensitivity of around 80%, and a specificity of 95%¹⁹. However, due to limited resources and the inability to order labs that deviated from the routine, the authors of this study never ordered the last two of these parameters; rather, they have just relied upon the routine tests and clinical signs and have achieved an even better AUC of 0.961. The use of bedside immunochromatographic kits for dengue detection of IgM, as studied in a Pakistan-based study, can aid in the calculation of the score mentioned earlier and potentially correct course while considering patients for intensive care, but requires an additional test in contrast to routine diagnostic testing, which includes only the NS1 antigen²⁰.

Although comorbid conditions were never a part of the final model in our study, a study done in Pakistan and Malaysia has highlighted that diabetes is a very strong risk factor for developing severe dengue²¹. A study during an endemic in Pakistan, on the other hand, has reported that clinical parameters such as rash, right hypochondrial tenderness, ascites and pleural effusion, and laboratory parameters including platelet count and a raised ALT were determinants of a complicated dengue infection²². Similarly, an Indonesian study has also reported that gall bladder thickness is useful in predicting the plasma leak in the coming days, with a sensitivity of 65%²³. Although this study has although it has employed

logistic regression and ROC analysis for predictive modeling, the inclusion of additional machine learning techniques or validation cohorts could strengthen the predictive models' reliability and performance metrics.

On the frontiers of mortality, a study done in Aga Khan Hospital stated that acute kidney injury, increasing age, and coagulopathy in patients with dengue virus infection is not only associated with a prolonged hospital stay but also lead to increased mortality²⁴. In our study, some patients with severe dengue developed acute kidney injury, but no mortality was seen, which may be attributable to the limited sample size. Another South East Asian study has come up with the proposition that during the first 3 days of illness, prognostic indicators should be platelet count or serum albumin. From the 4th - 6th day of illness, prognostic indicators should be AST, ALT, albumin, or total bilirubin²⁵.

CONCLUSION

In conclusion, this study has underscored the complexity of predicting severe dengue outcomes and highlighted both the strengths and limitations of current predictive markers. While certain clinical and laboratory parameters show promise as predictors, their utility varies widely, and additional research is needed to refine predictive models and enhance clinical decision-making. By integrating validated and low-cost predictors into routine clinical practice and fostering continuous research, healthcare providers can better manage dengue patients, optimize resource allocation, and improve patient outcomes.

CONFLICT OF INTEREST

None

FUNDING

None

ETHICAL APPROVAL

The study received ethical approval from the Ethical Review Committee of Ziauddin University Hospital under reference number 8540324QUME.

AUTHORS' CONTRIBUTIONS

QU: Concept and study design, data acquisition, manuscript writing, and final approval. **HYU:** Data acquisition, analysis, and interpretation. **YAR:** Data acquisition. **JMU:** Critical review and final approval.

REFERENCES

1. Ten health issues WHO will tackle this year [Internet]. [cited 2024 Apr 26]. Available from: <https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>.
2. Shaikh OA, Baig MT, Tahir S, Parekh ADE, Nashwan AJ. Dengue outbreak following unprecedented

- flooding in Pakistan. *Hygiene and Environmental Health Advances*. 2023 Sep;7:100076. doi: 10.1016/j.heha.2023.100076
3. Dengue - Global situation [Internet]. [cited 2024 Apr 26]. Available from: <https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON498>.
4. Khan U, Azeem S. The rising toll of dengue cases in Pakistan every year: An incipient crisis. *Ann Med Surg (Lond)*. 2022 Mar 31;76:103549. doi: 10.1016/j.amsu.2022.103549.
5. Goldman L, Schafer AI, editors. *Goldman-Cecil medicine*. 26th edition. Philadelphia, PA: Elsevier; 2020. 2 p.
6. Pajor MJ, Long B, Liang SY. Dengue: A focused review for the emergency clinician. *Am J Emerg Med*. 2024 Aug;82:82-87. doi: 10.1016/j.ajem.2024.05.022.
7. Waggoner JJ, Katzelnick LC, Burger-Calderon R, Gallini J, Moore RH, Kuan G, Balmaseda A, Pinsky BA, Harris E. Antibody-Dependent Enhancement of Severe Disease Is Mediated by Serum Viral Load in Pediatric Dengue Virus Infections. *J Infect Dis*. 2020 May 11;221(11):1846-1854. doi: 10.1093/infdis/jiz618.
8. Balingit JC, Denis D, Suzuki R, Hayati RF, Ngwe Tun MM, Takamatsu Y, Masyeni S, Sasmono RT, Morita K. Impact of pre-existing cross-reactive antibodies on cyclic dengue outbreaks in the hyperendemic region of Bali, Indonesia. *Virus Res*. 2024 Oct;348:199445. doi: 10.1016/j.virusres.2024.199445.
9. *Harrison's Principles of Internal Medicine*. 21st ed. New York: McGraw Hill; 2022.
10. Abraham PR, N PK, Kumar A. Dengue NS1 antigen kit shows high sensitivity for detection of recombinant dengue virus-2 NS1 antigen spiked with *Aedes aegypti* mosquitoes. *Scientific Reports*. 2021 Dec 8;11(1):23699. doi: 10.1038/s41598-021-02965-x
11. Prajapati A, Tandon A, Nain V. Towards the diagnosis of dengue virus and its serotypes using designed CRISPR/Cas13 gRNAs. *Bioinformatics*. 2022 Aug 31;18(8):661-668. doi: 10.6026/97320630018661.
12. Suwanto S, Nainggolan L, Sinto R, Effendi B, Ibrahim E, Suryamin M, Sasmono RT. Dengue score: a proposed diagnostic predictor for pleural effusion and/or ascites in adults with dengue infection. *BMC infectious diseases*. 2016 Dec;16:1-7. doi: 10.1186/s12879-016-1644-3.
13. Aftab S, Yaqoob E, Javed S. Dengue epidemic: Pakistan on alert. *The Lancet*. 2024 Nov ; 404 (10465) : 1807 . doi:10.1016/S0140-6736(24)02284-0
14. Tsai JF, Chu TL, Cuevas Brun EH, Lin MH. Solving Patient Allocation Problem during an Epidemic Dengue Fever Outbreak by Mathematical Modeling. *Healthcare (Basel)*. 2022 Jan 15;10(1):163. doi: 10.3390/healthcare10010163
15. Agrawal VK, Prusty BS, Reddy CS, Reddy GK, Agrawal RK, Bandaru VC. Clinical profile and predictors of Severe Dengue disease: A study from South India. *Caspian journal of internal medicine*. 2018;9(4):334. doi: 10.22088/cjim.9.4.334.
16. Hadinegoro SR. The revised WHO dengue case classification: does the system need to be modified? *Paediatr Int Child Health*. 2012 May;32 Suppl 1(s1):33-8. doi: 10.1179/2046904712Z.00000000052.
17. Aijan BA, Alafif MM, Alawi MM, Akbar NA, Aldigs EK, Madani TA. Assessment of the new World Health Organization's dengue classification for predicting severity of illness and level of healthcare required. *PLoS neglected tropical diseases*. 2019 Aug 20;13(8):e0007144. doi: 10.1371/journal.pntd.0007144.
18. Evaluation of the WHO 2009 classification for diagnosis of acute dengue in a large cohort of adults and children in Sri Lanka during a dengue-1 epidemic. *PLoS Negl Trop Dis*. 2018 Feb 9;12(2):e0006258. doi: 10.1371/journal.pntd.0006258.
19. Srisuphanunt M, Puttaruk P, Kooltheat N, Katzenmeier G, Wilairatana P. Correction: Srisuphanunt et al. Prognostic Indicators for the Early Prediction of Severe Dengue Infection: A Retrospective Study in a University Hospital in Thailand. *Trop. Med. Infect. Dis*. 2022, 7, 162. *Tropical Medicine and Infectious Disease*. 2022 Oct 31;7(11):339. 10.3390/tropicalmed7110339.
20. Kidwai AA, Ara J, Ghaznawi S, Rasheed SA, Paracha S, Hussain T. DENGUE RAPID DIAGNOSTIC TESTS:: EVALUATION OF UTILITY IN A TERTIARY CARE HOSPITAL. *The Professional Medical Journal*. 2017 Aug 8;24(08):1216-23. doi: 10.17957/TPMJ/17.3958
21. Riaz M, Harun SNB, Mallhi TH, Khan YH, Butt MH, Husain A, Khan MM, Khan AH. Evaluation of clinical and laboratory characteristics of dengue viral infection and risk factors of dengue hemorrhagic fever: a multi-center retrospective analysis. *BMC Infect Dis*. 2024 May 17;24(1):500. doi: 10.1186/s12879-024-09384-z.
22. Waheed I, Khalid S, Jamil Z. Predictors of complicated dengue infections in endemic region of Pakistan. *Asian Pacific Journal of Tropical Medicine*. 2022 Nov 1;15(11):496-502. doi: 10.4103/1995-7645.345554.
23. Nainggolan L, Wiguna C, Hasan I, Dewiasty E. Gallbladder Wall Thickening for Early Detection of Plasma Leakage in Dengue Infected Adult Patients. *Acta Med Indones*. 2018 Jul;50(3):193-199. PMID: 30333268.
24. Khalil MA, Tan J, Khalil MA, Awan S, Rangasami M. Predictors of hospital stay and mortality in dengue virus infection-experience from Aga Khan University Hospital Pakistan. *BMC Res Notes*. 2014 Jul 27;7:473. doi: 10.1186/1756-0500-7-473. PMID: 25064632; PMCID: PMC4115468.
25. Huy BV, Toan NV. Prognostic indicators associated with progresses of severe dengue. *PLoS One*. 2022 Jan 5;17(1):e0262096. doi: 10.1371/journal.pone.0262096. PMID: 34986174; PMCID: PMC8730386.