

Clinicopathological Parameters Affecting Hospital Stay in Dengue Fever

Hameer Saif Talpur, Ali Sufyan, Ahmed Farhan, Maria Zafar, Muhammad Safeer, Jawad Shafqat
Department of Medicine, Pakistan Institute of Medical Sciences, Islamabad

ABSTRACT

Objective: To identify clinical and laboratory parameters that can predict prolonged hospital stay and potentially severe disease in dengue patients, allowing for early triaging and appropriate resource allocation during epidemics when healthcare facilities in developing countries are often overburdened.

Methodology: This study was conducted at a Teaching hospital of Islamabad during the epidemic of Dengue fever 2023. After prior ethical approval, hospitalized dengue patients' demographic details, clinicopathological parameters and hospital stay were followed till patients were discharged. Data were analysed for association with hospital stay.

Results: A total of 182 hospitalized dengue patients were included in the study. Patients who developed a mean arterial pressure of <65 mmHg, pulse pressure of ≤ 20 mmHg, ALT ≥ 5 times upper limit of normal or advanced age were found to have a longer hospital stay. Patients who were vaccinated for COVID-19 were less likely to have a longer hospital stay; however, this association was close but not significant.

Conclusions: Advanced aged or those who developed hypotension, narrow pulse pressure or hepatic derangement need to be aggressively monitored in Dengue hospitalized patients as they are more likely to have to longer hospital stay.

Keywords: Alanine Transaminase, COVID-19, Dengue, Length of Stay, Severe Dengue.

Authors' Contribution:

^{1,2}Conception; Literature research; manuscript design and drafting; ^{3,4}Critical analysis and manuscript review; ^{5,6}Data analysis; Manuscript Editing.

Correspondence:

Ali Sufyan
Email: alisufyan92@gmail.com

Article info:

Received: September 11, 2024
Accepted: March 10, 2025

Cite this article. Talpur HS, Sufyan A, Farhan A, Zafar M, Safeer M, Shafqat J. Clinicopathological Parameters Affecting Hospital Stay in Dengue Fever. J Islamabad Med Dental Coll. 2025; 14(2). 158-163.
DOI: <https://10.35787/iimdc.v14i2.1293>

Funding Source: Nil
Conflict of interest: Nil

Introduction

Dengue fever is a disease with a wide range of symptoms and clinical presentation. It can present as simple dengue fever having no major clinical complication; to severe complications, which warranting hospital admission including admission to ICU as and when required.¹ Dengue fever has been reported in Pakistan since 1995 but recently emerging as a persistent and severe public health concern.^{2,3} The increasing frequency of outbreaks and the rising intensity of this mosquito-borne viral infection requires immediate national attention.⁴

The dengue virus has four known serotypes: DENV 1, DENV 2, DENV 3, and DENV 4. Each serotype can cause critical diseases, including Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).⁵ Between 2000 and 2019, a total of 201,269 cases were reported in Pakistan. The highest proportion of cases occurred in Khyber Pakhtunkhwa (KP) at 23.3%, followed by Punjab with 3.8% and Sindh at 1.9%. Among the reported dengue-infected cases, 74.4% were classified as Dengue Fever, 24.1% as Dengue Hemorrhagic Fever (DHF), and 1.5% as Dengue Shock Syndrome (DSS).⁶

In Pakistan, all four different serotypes have been reported in different outbreaks.⁷

Among hospitalized patients, a small proportion, approximately 10%, develop severe conditions i.e., severe dengue fever, Dengue Hemorrhagic Fever (DHF), or Dengue Shock Syndrome (DSS).⁵ These patients should be identified early and, ideally, admitted to an ICU for appropriate management. Patients admitted to the ICU with severe dengue typically present with two or more organ failures, which may manifest clinically, such as jaundice, reduced urine output, or coma or through abnormal laboratory findings. Two critical markers for assessing reduced peripheral and organ perfusion are capillary refill time and serum lactate levels.⁸ Pakistan, like many tropical and subtropical regions, is met with recurrent epidemics of dengue, thus increasing the need for a more profound understanding of the different clinicopathological variables that influence the progression of disease in host and community.

This study aims to grasp the complexity of disease by observing a range of influencing factors such as epidemiological patterns, environmental conditions, host characteristics, and the behavior of the dengue virus itself. By analyzing these elements collectively, the research aims to highlight, how to improve preventive measures, diagnosis, and management of dengue in Pakistan. This understanding is vital for crafting effective interventions to tackle the ongoing health crisis facing the country.

Methodology

This prospective study was conducted at Pakistan Institute of Medical Sciences, Islamabad during the epidemic of Dengue fever 2023. This hospital receives one of the highest cases of Dengue in the region. The research was conducted at Medical Ward 6 of the Pakistan Institute of Medical Sciences (PIMS) in Islamabad, where 182 patients diagnosed with dengue fever were observed over a span of three months. We examined various factors such as

age, COVID vaccination status, platelet counts, haematocrit levels, total leukocyte counts, mean arterial pressure (MAP), pulse pressure, and duration of hospital stay. By a thorough analysis, we aimed to uncover patterns in these variables and their implications for managing dengue fever effectively. Ultimately, our findings hold the potential to improve patient care and inform more robust public health strategies in Pakistan's ongoing struggle against this challenging illness. Patients who were admitted with confirmation of Dengue via Clinical as well as Laboratory criteria were included. While following standard of care as per institutional protocols patients' demographic details including age, gender, date of admission, COVID-19 vaccination status was recorded. Patients' clinical parameters including Mean arterial pressure (MAP), Pulse pressure (PP), Dengue diagnosis type as well as laboratory parameters including Alanine Transaminase (ALT) were noted. Patients were followed till discharge noting length of hospital stay. Data was entered and analysed using IBM SPSS version 25. Categorical variables as Gender, COVID-19 vaccination status, MAP category, PP category, Length of hospital stay category, ALT category were represented as frequencies and percentages. Continuous variables as Age was represented as mean and standard deviation. Cross tables were formulated with variables comparing with length of hospital stay. Chi square and independent sample t-test were employed to assess the strength of association while considering p value of less than 0.05 as significant.

Ethical approval was sought through the Ethical Review Board (ERB) of PIMS hospital (No.F.3-1/2023(ERB)/Chairman) dated 17-11-2023.

Results

A total of 182 hospitalized dengue patients were included in the study. The mean age was $36.12 \pm$

Parameters		Total Hospital		P value
		≤ 72 hrs	> 72 hrs	
		% (N)	% (N)	
ALT levels	ALT <5x ULN	63.1 (94)	36.9 (55)	0.003
	ALT 5x ULN or more	41.4 (12)	58.6 (17)	
Pulse Pressure	Pulse pressure >20 mmHg	72.9 (97)	27.1 (36)	<0.001
	Pulse pressure ≤20 mmHg	20.0 (9)	80.0 (36)	
Mean Arterial Pressure (MAP)	MAP >65 mmHg	67.1 (100)	32.9 (49)	<0.001
	MAP ≤65 mmHg	17.9 (5)	82.1 (23)	
COVID Vaccination status	Unvaccinated	50.8 (31)	49.2 (30)	0.087
	Vaccinated	64.1 (75)	35.9 (42)	
Diagnosis	Classic Dengue	84.8 (56)	15.2 (10)	<0.001
	DHF1	62.3 (43)	37.7 (26)	
	DHF2	13.8 (4)	86.2 (25)	
	DSS	33.3 (2)	66.7 (4)	
	Expanded Dengue	12.5 (1)	87.5 (7)	
Age (mean)		33	41	<0.001

14.56 years and 70.9% (n=129) were male while 29.1% (n=53) were female. Details of baseline characteristics of patients are given in Table II. Patients that had a decrease in Mean Arterial Pressure (MAP) of less than 65mmHg, Alanine Transaminase (ALT) of more than 5 times the upper limit normal, Pulse pressure less than 20mmHg and advancing age were more likely to longer hospital stay. This association was statistically significant. Details of parameters in relation to hospital stay are given in Table I.

Patient characteristics	% (N)
Age	
Mean ± SD	36.12 ± 14.56 years
Gender	
Male	70.9 (129)
Female	29.1 (53)
Hospital stay	
72 hrs. or less	58 (106)
Greater than 72 hrs.	39.6 (72)
Dengue Diagnosis	
Classic Dengue	37.4 (68)
Dengue Haemorrhagic Fever I (DHF I)	39.0 (71)
Dengue Haemorrhagic Fever II (DHF II)	15.9 (29)
Dengue Shock Syndrome	3.3 (6)
Expanded Dengue Syndrome	4.4 (8)

Discussion

Current study had a population of relatively young individuals with results comparable to national and international published studies.^{9,10} Evaluation of the demographics of our study showed a higher population of males as compared to females. Our study results are comparable with results published by Khalil et. al. as well as Willeam et. Al.^{11,12} A local study done by Anjum et. al. reported similar male to female ratios.¹³ On the contrary Fonseca-Portilla et. al. reported a study population comprising a large of females.¹⁴ This difference in population might have been raised from the difference of local populations. Our study showed that a higher age was associated with longer stay. As table I depicts, the Mean ages were found to be higher in patients with a hospital of more than 72 hours or 3 days. (p value ≤0.001) Our study was in agreement with Kaleem et. al. as they also reported that a longer stay was associated with higher ages.¹⁵ Rowe et. al. also published similar findings in his article concluding that elderly were at higher risk of getting a severe disease than young

population.¹⁶ These findings are also comparable to the work of Recker et. al., da Silva et.al. and Khalil et al.¹⁷⁻¹⁹

Almost one-third of the population presented with Dengue Hemorrhagic fever (type 1 and 2 combined) while the rest had classic dengue syndrome. Only a small number of patients presented with Dengue shock or dengue expanded syndrome. While Prattey et al. reported that a much higher number of patients presented with classical dengue rather than DHF.²⁰ Likewise, Mallhi et al. also reported that majority of the study population was diagnosed with classical dengue fever, with DHF and DSS comprising only a small percentage.²¹

We also observed multiple factors affecting the overall hospital stay in study patients. It was observed that a large number of patients having a serum ALT level of less than 5 times the upper limit, were discharged with 3 days of admission as compared to those having ALT values of more than or equal to 5 times (p value 0.003). The findings of current study are comparable with the findings reported by Shahin and Aly et al.²² Mushtaq et al. in his study stated that patients with a more severe disease had a significant rise in both AST and ALT, with a more marked rise in AST than ALT.⁹ A large meta-analysis also supports our findings.²³ Ho et al. also demonstrated that liver enzymes derangements were associated with severe dengue thus increasing hospital stay.²⁴ Likewise, findings from studies by Srisuphanunt et al., Aroor et al., Sachdev et al., Khan et al and Fida et al. reported that elevated levels of liver enzymes are correlated with heightened severity of dengue and prolonged hospitalization durations.²⁵⁻²⁸ In contrast to our study Willeam peter et al. observed no significant difference with respect to deranged liver enzymes when compared for hospital stay.¹²

The present study identified a statistically significant correlation between both pulse pressure and mean arterial pressure (MAP) with length of hospital stay. It was also observed that patients having pulse pressure of less than 20 mmHg stayed more as

compared to those who had a pulse pressure of more than 20 mmHg (p value <0.001). Similarly, patients who had lower Mean Arterial Pressure MAP had a similar effect on hospital stay, as those experiencing hypotension with MAP less than 65 mmHg stayed much than the participants who did not experience any hypotension and were discharged within 3 days of admission. (p value <0.001). However, a comprehensive literature review revealed limited research on this specific association, highlighting the need for further investigation in this area.

Patients unvaccinated against COVID-19 had a longer stay as compared to those having vaccinations but this wasn't statistically significant although very close to being significant (p value 0.087). A higher number of Patients with Dengue Fever and DHF 1 were discharged in first 3 days while patients having DHF 2, Dengue shock or dengue expanded remained admitted for more than 3 days as described in the table above. In contrast to our study, a study done in Indonesia by Arianti et al. did not report statistically significant correlation of hospital stay with age and other different variables.²⁹

Limitations of study include a single centered study; it is thus recommended to conduct a multi centered study over a larger scale population. Moreover, patients may be followed up after discharge to note down the possible improvement in parameters post discharge.

Conclusion

- Advanced aged, those who develop hypotension, narrow pulse pressure or hepatic derangement are the factors associated with prolonged hospital stay in Dengue patients and need to be vigilantly monitored.
- There might be a protective effect of COVID-19 vaccination on Dengue complications which requires further validation through larger scale studies

References

1. Khan MIH, Anwar E, Agha A, Hassanien NSM, Ullah E, Syed IA, et al. Factors predicting severe dengue in patients with dengue fever. *Mediterr J Hematol Infect Dis*. 2013;5(1):e2013014. <https://doi.org/10.4084/mjhid.2013.014>
2. Rasheed SB, Butlin RK, Boots M. A review of dengue as an emerging disease in Pakistan. *Public Health*. 2013;127(1):117. <https://doi.org/10.1016/j.puhe.2012.09.006>
3. Akram DS, Igarashi A, Takasu T. Dengue virus infection among children with undifferentiated fever in Karachi. *Indian J Pediatr*. 1998;65(5):735-40. <https://doi.org/10.1007/bf02731055>
4. Zohra T, Din M, Ikram A, Bashir A, Jahangir H, Baloch IS, et al. Demographic and clinical features of dengue fever infection in Pakistan: a cross-sectional epidemiological study. *Trop Dis Travel Med Vaccines*. 2024;10(1):11. <https://doi.org/10.1186/s40794-024-00221-4>
5. Bhalla A, Singh H, Suri V, Yaddanapudi L, Poddar B, Ghawat R, et al. ISCCM position statement: management of severe dengue in intensive care unit. *Indian J Crit Care Med*. 2024;28(Suppl 2):S42.
6. Khattak A, Khan S, Ali I, Gul A, Khabir MN, Javed B, et al. Burden and distribution of dengue infection in Pakistan (2000-19): a review. *Braz J Biol*. 2023;84:e267982.
7. Haroon M, Jan H, Faisal S, Ali N, Kamran M, Ullah F. Dengue outbreak in Peshawar: clinical features and laboratory markers of dengue virus infection. *J Infect Public Health*. 2019;12(2):258-62. <http://dx.doi.org/10.1016/j.jiph.2018.10.138>
8. Kattan E, Hernández G. The role of peripheral perfusion markers and lactate in septic shock resuscitation. *J Intensive Med*. 2021;2(1):17-21. <http://dx.doi.org/10.1016/j.jointm.2021.11.002>
9. Mushtaq S, Khan MIU, Khan MT, Husain A. Demographic and clinical variables in the dengue epidemic in Punjab, Pakistan. *Pak J Med Sci*. 2023;39(6):17426. <https://doi.org/10.12669/pjms.39.6.7383>
10. Vicente CR, Junior CC, Fröschl G, Romano CM, Cabidelle ASA, Herbingler KH. Influence of demographics on clinical outcome of dengue: a cross-sectional study of 6703 confirmed cases in Vitória, Espírito Santo State, Brazil. *Epidemiol Infect*. 2017;145(1):46-53. <https://doi.org/10.1017/S0950268816002004>
11. Khalil MAM, Tan J, Khalil MAU, 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;7:473. <https://doi.org/10.1186/1756-0500-7-473>
12. Willeam Peter SS, Hassan SS, Khei Tan VP, Ngim CF, Azreen Adnan NA, Pong LY, et al. Admission clinicopathological factors associated with prolonged hospital stay among hospitalized patients with dengue viral infections. *Vector Borne Zoonotic Dis*. 2019;19(7):549-52. <https://doi.org/10.1089/vbz.2018.2379>
13. Anjum A, Assad AA, Sadia A, Maimoona A, Sarwar S. Dengue hemorrhagic fever: risk factors in Pakistani cohort. *Ann King Edward Med Univ*. 2024;30(1). <https://doi.org/10.21649/akemu.v30i1.5494>
14. Fonseca-Portilla R, Martínez-Gil M, Morgenstern-Kaplan D. Risk factors for hospitalization and mortality due to dengue fever in a Mexican population: a retrospective cohort study. *Int J Infect Dis*. 2021;110:332-6. <https://doi.org/10.1016/j.ijid.2021.07.062>
15. Kaleem Z, Waris MH, Muneer R, Malik MN, Akram A, Ghazanfar S, et al. Predictors of hospital stay and prognostic factors for dengue infection in Holy Family Hospital, Rawalpindi. *J Popul Ther Clin Pharmacol*. 2023;30(18):995-1000. <https://doi.org/10.53555/jptcp.v30i18.3218>
16. Rowe EK, Leo YS, Wong JGX, Thein TL, Gan VC, Lee LK, et al. Challenges in dengue fever in the elderly: atypical presentation and risk of severe dengue and hospital-acquired infection. *PLoS Negl Trop Dis*. 2014;8(4):e2777. <https://doi.org/10.1371/journal.pntd.0002777>
17. Recker M, Fleischmann WA, Nghia TH, Truong NV, Nam LV, Anh DD, et al. Markers of prolonged hospitalisation in severe dengue. *PLoS Negl Trop Dis*. 2024;18(1):e0011922. <https://doi.org/10.1371/journal.pntd.0011922>
18. da Silva NS, Undurraga EA, da Silva Ferreira ER, Estofolete CF, Nogueira ML. Clinical, laboratory, and demographic determinants of hospitalization due to dengue in 7613 patients: a retrospective study based on hierarchical models. *Acta Trop*. 2018;177:25-31. <https://doi.org/10.1016/j.actatropica.2017.09.025>
19. Khalil MAM, Tan J, Khalil MAU, 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;7:473. <https://doi.org/10.1186/1756-0500-7-473>
20. Prattay KMR, Sarkar MR, Shafiullah AZM, Islam MS, Raihan SZ, Sharmin N. A retrospective study on the socio-demographic factors and clinical parameters of dengue disease and their effects on the clinical course and recovery of the patients in a tertiary care hospital of Bangladesh. *PLoS Negl Trop Dis*. 2022;16(4):e0010297. <https://doi.org/10.1371/journal.pntd.0010297>

21. Mallhi TH, Khan AH, Sarriff A, Adnan AS, Khan YH. Determinants of mortality and prolonged hospital stay among dengue patients attending tertiary care hospital: a cross-sectional retrospective analysis. *BMJ Open*. 2017;7(7):e016805. <https://doi.org/10.1136/bmjopen-2017-016805>
22. Shahin W, Aly M. Predictors of death and prolonged hospital length of stay in dengue fever patients admitted to a tertiary hospital in Makkah. *Afro-Egypt J Infect Endem Dis*. 2013;3(4):127-34. <https://doi.org/10.21608/aeji.2013.18255>
23. Yuan K, Chen Y, Zhong M, Lin Y, Liu L. Risk and predictive factors for severe dengue infection: a systematic review and meta-analysis. *PLoS One*. 2022;17(4):e0267186. <https://doi.org/10.1371/journal.pone.0267186>
24. Ho TS, Wang SM, Lin YS, Liu CC. Clinical and laboratory predictive markers for acute dengue infection. *J Biomed Sci*. 2013;20:75. <https://doi.org/10.1186/1423-0127-20-75>
25. Sachdev A, Pathak D, Gupta N, Simalti A, Gupta D, Gupta S, et al. Early predictors of mortality in children with severe dengue fever: a prospective study. *Pediatr Infect Dis J*. 2021;40(9):797-802.
26. Aroor AR, Saya RP, Sharma A, Venkatesh A, Alva R. Clinical manifestations and predictors of thrombocytopenia in hospitalized adults with dengue fever. *North Am J Med Sci*. 2015;7(12):547-52. <http://doi.org/10.4103/1947-2714.172841>
27. Srisuphanunt M, Puttaruk P, Kooltheat N, Katzenmeier G, Wilairatana P. 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(8):162. <https://doi.org/10.3390/tropicalmed7080162>
28. Fida Z, Khan Z, Khan A, Khan H, Rahman FU. Outcome of patients with dengue fever. *Gomal J Med Sci*. 2016;14(3). Available from: <https://www.gjms.com.pk/index.php/journal/article/view/672>
29. Arianti MD, Prijambodo J, Wujoso H. Relationships between age, sex, laboratory parameter, and length of stay in patients with dengue hemorrhagic fever. *J Epidemiol Public Health*. 2019;4(4):307-13. <http://doi.org/10.26911/jepublichealth.2019.04.04.05>