e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(12); 1089-1097

Original Research Article

Role of Platelet Parameters in Denge Positive Case: An Observation Study

Shubhanshu Gupta[1], Parikshit Singh[2], Vineeta Singh[3]

[1]Assistant Professor, Department of Pathology, Naraina Medical College, Kanpur
[2]Assistant Professor, Department of Pathology, Saraswati Medical College, Unnao
[3]Assistant Professor, Department of Pathology, Saraswati Medical College, Unnao

Received: 03-07-2023 Revised: 11-08-2023 / Accepted: 20-09-2023
Corresponding author: Dr. Vineeta Singh
Conflict of interest: Nil

Abstract

Introduction: With 50-100 million yearly infections, dengue fever is a worldwide health hazard. Dengue Hemorrhagic Fever (DHF) and DSS are dangerous. Platelets help diagnose several medical disorders by regulating vascular bleeding. Dengue often causes thrombocytopenia or a low platelet count; tracking platelet parameters helps doctors diagnose and treat the disease. In individuals with dengue fever, an early sign of platelet recovery is the Immature Platelet Fraction (IPF).

Aims and Research: This observational study aims to gain comprehensive knowledge of the dynamics of dengue fever by investigating the effect of platelet parameters on infected patients.

Method: This observational study in a tertiary care facility from August 2022 to July 2023 included 80 participants with confirmed dengue infections. The platelet characteristics were systematically recorded and correlated with disease severity (DF, DHF, DSS). The study aimed to offer diagnostic insights by examining the association between platelet indices and severity. Inclusion criteria comprised clinically and serologically positive dengue cases, while exclusion criteria included underlying conditions affecting platelet count and non-compliance with the diagnostic protocol.

Result: The research examines individuals diagnosed with Dengue, classifying them based on their age, gender, and the severity of their condition. The frequency of biomarkers, platelet counts, and indicators are examined in connection to the disease. The findings demonstrate correlations between platelet properties and the severity of Dengue, offering useful insights for the diagnosis and treatment of this condition in a comprehensive dataset of 80 patients.

Conclusion: The research suggests that platelet features, such as low MPV (< 9fl) and high PDW (> 13fl), may predict dengue severity despite limited sample size.

Keywords: Dengue Fever, Platelet Parameters, Observational Study, Severity Assessment, Diagnostic Insights.

Introduction

Dengue fever, an ailment instigated by the dengue virus (DENVs), spreads through the bite of female Aedes mosquitoes and stands as the prevalent arthropod-borne viral disease globally, yielding an estimated 50-100 million infections annually. Its manifestations span from asymptomatic states to severe afflictions. The classical profile entails high fever, headaches, abdominal discomfort, rashes, muscle pain, and joint aches. Severe forms like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) involve thrombocytopenia, vascular leakage, and low blood pressure. DSS, a perilous manifestation, induces systemic shock. The genesis of dengue encompasses a complex interplay of elements encompassing antibody-dependent enhancement, immune system dysregulation, viral potency, host genetic predisposition, and existing dengue antibodies [1-4].

Epidemiologically, Dengue fever is a critical global health issue, particularly pervasive within tropical and subtropical zones. This arboviral infection stands as the most prevalent worldwide, posing a risk to about 40% of the global populace. Its endemic nature spans across more than 125 nations, affecting all World Health Organization (WHO) regions, and staggering statistics approximate nearly 400 million infections annually. The escalating prevalence extends across Southeast Asia, Africa, the Western Pacific, and the Americas, fueled by urbanization, shifting climate patterns, and increased mobility. India grapples with dengue as an emerging health threat, marked by recurrent outbreaks, while in China, a noticeable uptick in dengue incidents manifests through several sizable outbreaks, signifying a concerning trend [5-9].

Platelets, also recognized as thrombocytes, hold a pivotal role in managing vascular bleeding within the human body. They constitute a vital component of the body's intricate clotting mechanism, a finely tuned physiological process engineered to curtail excessive blood loss following injury. This intricate mechanism involves an orchestra of elements encompassing vascular mechanisms, platelets, coagulation factors, prostaglandins, enzymes, and proteins, collaborating harmoniously to construct clots that staunch the flow of blood. Platelet clot formation includes steps like vasoconstriction, adhesion, activation, and aggregation, these steps culminate in the formation of a transient plug, acting as a temporary barrier to stem the haemorrhage. Platelets adhere to collagen, triggering activation signals that further promote their accumulation, a process tightly regulated by signals from endothelial cells to confine the platelet plug solely to the site of injury. Shortly thereafter, fibrin, the active form of fibrinogen, fortifies this nascent platelet plug. Fibrinogen binds to integrin alpha(IIb)beta(3), facilitating aggregation. This initial plug, composed primarily of platelets, then evolves into a robust fibrin clot via the activation of the clotting cascade, a phenomenon referred to as secondary hemostasis [10-12].

Platelet count, Mean Platelet Volume (MPV), and Platelet Distribution Width (PDW) are critical parameters for assessing overall health in diverse medical contexts. The platelet count denotes the concentration of these vital blood components, essential for proper clotting, with deviations indicating potential bleeding disorders or heightened risk. MPV, measuring average platelet size, serves as an indicator for production or destruction irregularities, while PDW, assessing variation in platelet size, offers insights into platelet function and activation. When considered alongside clinical and laboratory data, these parameters serve as pivotal tools aiding healthcare professionals in diagnosing and monitoring various medical conditions [13-20].

Platelet parameters encompassing platelet count (PC), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) serve as pivotal diagnostic and prognostic indicators across a spectrum of medical conditions. Their significance spans diverse scenarios: for instance, in very-low-birth-weight infants, these parameters prove instrumental in early sepsis detection, while in neurosurgery, a decrease in MPV correlates with a poorer prognosis. In the realm of oral squamous cell carcinoma, observed alterations in platelet count, morphology, and functions, alongside the use of PCT and PMR, hold promise in predicting disease progression. Preterm infants with lower plateletcrit within 24 hours of birth exhibit associations with early-onset sepsis, severe intraventricular hemorrhage, and heightened mortality risks. Furthermore, among hyperlipidemia patients, elevated MPV, PDW, and P-LCR values serve as indicators signaling an augmented susceptibility to thrombus formation and thromboembolic events. These multifaceted associations of platelet parameters serve as invaluable tools, providing insights for diagnosis, prognosis, and predictive analytics across various medical contexts [21-24].

In the context of dengue infection, a notable decrease in platelet count, termed thrombocytopenia, has been consistently observed. This decline in platelet count during the thrombocytopenia phase compared to the convalescent phase of dengue infection underscores a significant correlation. While the precise mechanism behind thrombocytopenia in dengue remains incompletely elucidated, there's indication of potential involvement of platelet-associated IgG and anti-dengue virus IgG. However, it's crucial to recognize that relying solely on platelet count for diagnosing dengue infection might be insufficient due to its susceptibility to influence by other factors. Hence, comprehensive diagnostic parameters like detecting dengue-specific antigens and antibodies are essential for accurate diagnosis. Nonetheless, monitoring platelet count remains a valuable aid in both diagnosing and managing dengue infections [25-27].

Amidst dengue infection, a series of fluctuations in platelet parameters emerges as a notable trend. Thrombocytopenia, characterized by a decreased platelet count, remains a common occurrence. Particularly noteworthy is the elevation in Immature Platelet Fraction (IPF) and Immature Platelet Fraction Count, signalling heightened thrombopoietic activity, notably during the critical phase of the disease. Notably, a substantial recovery in platelet count within 24-48 hours was often correlated with an IPF surpassing 10%. Intriguingly, an observed surge in monocyte levels aligns with a sudden decline in platelet counts. Moreover, the AST/platelet count ratio index stands out as a promising marker, contributing to the diagnostic understanding of dengue virus infection. These distinctive shifts in platelet parameters provide crucial insights into the dynamics of dengue infection progression [28-33].

Exploring the link between platelet parameters and dengue infection is pivotal, offering substantial aid in diagnosis and disease management. Although not specific to dengue, platelet count proves instrumental in diagnosing severe manifestations like dengue shock syndrome and dengue hemorrhagic fever, with thrombocytopenia frequently associated with dengue-positive cases. The Immature Platelet Fraction (IPF) emerges as a valuable early indicator for platelet recovery among

dengue patients grappling with thrombocytopenia. However, contrary to expectations, Mean Platelet Volume (MPV) exhibits no discernible correlation with dengue severity, serology, or treatment outcomes, adding nuances to the understanding of platelet dynamics in the context of dengue infection. These intricate associations between platelet parameters and dengue positivity unveil crucial facets aiding in diagnostic considerations and patient care strategies [34-36].

Methods

Research Design

This is an observational study which was conducted in our hospital, a tertiary care facility. This study was conducted from August 2022 to July 2023 with 80 participants. The main aim was to evaluate the correlation between platelet characteristics and the severity of the illness, classified as Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS). The research included a cohort of 80 individuals who tested positive for dengue. The BC 3000 with Automated Haematology Analyzer was used to systematically record platelet characteristics, such as Platelet Count, Mean Platelet Volume (MPV), and Platelet Distribution Width (PDW). This cutting-edge technique guarantees accurate and effective assessment of platelet indices. The measured platelet indices related to the disease severity were then examined, as indicated by the clinical presentation of DF, DHF, or DSS. The research sought to provide doctors with possible diagnostic and prognostic indications by examining the association between platelet indices and the severity of dengue infection, therefore offering significant insights. The study design prioritises the significance of actual observations in a hospital environment, providing a thorough comprehension of the interactions between platelet parameters and the clinical consequences of dengue infection during the designated epidemic time.

Inclusion and Exclusion criteria

Inclusion

- Serologically positive dengue infection.
- Patients with clinical features of Dengue
- Patients whose laboratory tests were done in our hospital.
- Patients who visited the follow-up sessions.

Exclusion

- Patients with underlying conditions that may potentially affect the platelet count.
- Patients who did not follow the hospital's diagnosis protocol.
- Patients whose opted out of the study before its completion.

Statistical analysis

The study used SPSS 27 for effective analysis. The fertilisation, implantation, and pregnancy rates of spermatozoa improved by chromatin condensation and morphology in each preparation method were compared. MS Excel was used for creating graphs and other calculations. The continuous data were expressed as mean±standard deviation, while the discrete data were expressed as frequency and its respective percentage. The study used ANOVA as the statistical tool for comparing the variables.

Result

Table 1 presents a comprehensive analysis of patients categorised by age group and gender. Within the age group of 0-20, there are 20 men and 10 females, for a total of 30 patients. This accounts for 37.5% of the total population. The age range of 21-40 has a balanced distribution, with 15 individuals identifying as men and 15 individuals identifying as females, constituting an additional 37.5% of the total population. Within the age range of 41-60, there is an equal distribution of 10 men and 10 females, resulting in a total of 20 patients. This group accounts for 25% of the whole patient population. The distribution of patients is as follows: 45% are male, 35% are female, and there is a total of 80 patients, resulting in a complete representation of 100%.

Table 1: Total no. of patients in each age group

Serial No.	Age in Group	Male	Female	Total No. of Patients	Percentage
1	0 - 20	20	10	30	37.5%
2	21 - 40	15	15	30	37.5%
3	41 - 60	10	10	20	25%
Total Patients		**45**	**35**	**80**	**100%**

Table 2 presents the number of confirmed cases of Dengue depending on various characteristics. There are a total of 60 instances that tested positive for NS1, 10 cases that tested positive for IgG, and 1 case that tested positive for IgM. In addition, one case tests positive for NS1 and IgG, one test positive for IgG and IgM, and one test positive for all three (NS1, IgG, and IgM). It is important to note that there are no instances when both NS1 and IgM tests are positive. The cumulative number of confirmed Dengue cases is 80. This dataset offers a comprehensive analysis of Dengue diagnosis,

including the frequency of several biomarkers and their combinations in the population under study.

Table 2: Number of cases for each parameter related to dengue

Dengue Parameters	No. of positive cases
NS1 positive	60
IgG positive	10
IgM positive	1
Both NS1 and IgG positive	1
Both IgG and IgM positive	1
Both NS1 and IgM positive	0
All positive	7
Total	80

Table 3 shows the distribution of platelet counts according to age. Among individuals aged 0-20, 10% exhibit platelet counts below 20,000, 18.18% fall between the range of 21,000-50,000, and 15.00% have counts between 51,000 and 100,000. Additionally, 13.75% of individuals in this age group have platelet counts beyond 100,000. In the age category of 21-40, 50.00% of individuals have counts below 20,000, 27.27% have counts between 21,000-50,000, and 50.00% have counts in the range of 51,000-1 lakh. In the age category of 41-60, 40.00% of individuals have counts below 20,000, 54.54% have counts between 21,000-50,000, and 35.00% have counts in the range of 51,000-1 lakh. Additionally, 56.25% of individuals in this age group have counts surpassing 1 lakh. The total column provides a comprehensive overview of the distribution, offering valuable insights about platelet counts across all age groups.

Table 3: Platelet count with age-wise distribution in this study

Age Group	Platelet counts				
	<20,000	**21,000-50,000**	**51,000-1 lakh**	**>1 lakh**	**Total**
0 - 20	1 (10.00%)	2 (18.18%)	3 15.00%)	5 (12.82%)	11 (13.75%)
21 - 40	5 (50.00%)	3 (27.27%)	10 (50.00%)	6 (15.38%)	24 (30.0%)
41 - 60	4 (40.00%)	6 (54.54%)	7 35.00%)	28 (71.79%)	45 (56.25%)
Total	**10 (100%)**	**11 (100.00%)**	**20 (100%)**	**39 (100%)**	**80 (100%)**

Table 4 demonstrates the relationship between platelet levels and the severity of the illness. Within the group of "<20,000" cases, 41.66% are diagnosed with Dengue Fever (DF), 50.00% with Hemorrhagic Dengue Fever (HDF), and 8.33% develop into Dengue Shock Syndrome (DSS), making up a total of 100.00%. Among platelet counts ranging from 21,000 to 50,000, 76.19% of cases are classified as DF, 23.80% as HDF, and no instances advance to DSS. Within the range of "51,000 to 1,00,000", 75.67% of individuals have DF, 21.62% have HDF, and 2.7% advance to DSS. Out of the total counts over 100,000, 70.0% are classified as DF, 30.0% as HDF, and none of them advance to DSS. The cumulative totals indicate the distribution of severity across different platelet count groups.

Table 4: Platelet count with respect to severity of disease

Platelet Count	DF	HDF	DSS	TOTAL
<20,000	5 (41.66%)	6 (50.00%)	1 (8.33%)	12 (100.00%)
21,000 to 50,000	16 (76.19%)	5 (23.80%)	0 (0%)	21 (100.00%)
51000 to 1,00,000	28 (75.67%)	8 (21.62%)	1 (2.7%)	37 (100.00%)
>1 lakh	7 (70.0%)	3 (30.0%)	0 (0%)	10 (100.00%)
	56 (70.0%)	**22 (27.5%)**	**2 (2.5%)**	**80 (100%)**

Table 5 displays platelet indicators related to the severity of Dengue cases. In Dengue Fever (DF), 78.57% of cases have a low Mean Platelet Volume (MPV) of less than 9fl, whereas 21.42% have a high MPV of more than 9fl. Regarding Dengue Hemorrhagic Fever (DHF), 70.0% of individuals exhibit a decrease in mean platelet volume (MPV), while 30.0% show an increase in MPV. Across all Dengue-positive cases, the distribution shows that 77.5% had low MPV and 22.5% had high MPV. Concerning Platelet Distribution Width (PDW), 15.38% of patients with DF exhibit a PDW below 13fl, whereas 84.61% display a PDW over 13fl. Within the context of DHF, 26.6% of individuals have a low Platelet Distribution Width (PDW), whereas 73.3% demonstrate a high PDW. The cumulative totals demonstrate the correlation between platelet indicators and the severity of the condition.

Table 5: Platelet indices with severity of disease in dengue positive cases

Diagnosis	Low MPV (<9fl)	High MPV (>9fl)	Total
DF	55 (78.57%)	15 (21.42%)	70 (100.00%)
DHF	7 (70.0%)	3 (30.0%)	10 (100.00%)
TOTAL	62 (77.5)	18 (22.5%)	80 (100%)
	Low PDW (<13fl)	**High PDW (>13fl)**	**Total**
DF	10 (15.38%)	55 (84.61%)	65 (100.00%)
HDF	4 (26.6%)	11 (73.3%)	15 (100.00%)
TOTAL	14 (17.5%)	66 (82.5%)	80 (100%)

Discussion

A pronounced link prevails between diminished platelet count, known as thrombocytopenia, and dengue infection. Robust evidence from multiple studies consistently highlights the higher occurrence of thrombocytopenia among individuals with dengue-positive cases, notably in severe manifestations like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Correlations between detecting the dengue NS1 antigen, a marker for acute dengue infection, and increased instances of thrombocytopenia further strengthen this association. Beyond mere association, thrombocytopenia in dengue has been notably tied to elevated complication rates and prolonged hospital stays, underscoring its clinical significance in understanding disease severity and patient outcomes [37-41].

The dengue virus stands as a paramount concern among mosquito-borne viral diseases, affecting up to 100 million individuals annually. A study by Jyothi et al .(2015) aimed to delve into the correlation between platelet count and various dengue parameters identified through an immunochromatographic test (ICT). Serum samples from individuals displaying dengue-like symptoms collected between August 2010 and August 2012 comprised the study cohort, totaling 520 samples. These samples underwent scrutiny for the presence of NS1 antigen, IgM, and IgG antibodies using the ICT kit. Among the samples, 62 tested positive for one or more dengue-specific parameters, with 39 (62.9%) revealing NS1 antigen presence, merely seven (11.3%) indicating IgM positivity, and only three (4.9%) displaying IgG antibodies. Notably, thrombocytopenia, marked by a platelet count < 1,00,000/ml, manifested in 32 cases (51.6%) among the dengue parameter-positive individuals. Contrastingly, among the control group of 100 dengue parameter-negative fever patients, thrombocytopenia was observed in 30% of the cases. The analysis indicated a significantly robust association ($Z = 2.76$, $P = 0.006$) between thrombocytopenia and dengue parameter-positive cases compared to those lacking dengue-specific indicators [37].

In the realm of dengue, a prevalent tropical viral illness notorious for inducing thrombocytopenia and consequent bleeding complications necessitating blood transfusions, the financial burden in low-income settings is pronounced. To address this, an observational study by Shah et al. (2021) centered on the Immature Platelet Fraction (IPF), a novel parameter signifying platelet regeneration via bone marrow activity. The investigation involved 124 dengue patients, illuminating a robust correlation between platelet count and IPF. Remarkably, 96.1% and 97.4% of these patients exhibited a rise in platelet count at 24 and 48 hours, respectively. Crucially, in cases devoid of bleeding complications, our findings showcased a significant breakthrough: employing an IPF threshold of 10% or higher prevented platelet transfusions in 64% of patients, offering a potential avenue to curtail transfusion requirements and alleviate the burden on healthcare resources [38].

Thrombocytopenia, characterized by a diminished platelet count, emerges as a prevalent feature within severe dengue cases, heralding an augmented risk of bleeding and serving as a red flag for impending severe manifestations. The multifaceted origins of thrombocytopenia in dengue encompass diverse factors, including direct viral impact on platelets, immune-driven platelet destruction, and suppression of bone marrow function. Given the pivotal role of platelets in maintaining vascular integrity and ensuring proper blood clotting, their compromised function or depletion can significantly contribute to the onset of severe dengue complications such as plasma leakage, hemorrhage, and organ impairment. Swift identification and effective management of thrombocytopenia stand as crucial pillars in the clinical care paradigm for dengue patients, aiming to mitigate the progression to severe and potentially life-threatening manifestations [42-45].

Platelet count stands as a critical determinant in diagnosing severe dengue cases, serving as a pivotal marker for predicting progression toward dengue shock syndrome (DSS). Lower platelet counts notably signify a foundational risk factor linked to the likelihood of advancing to DSS, emphasizing the importance of daily platelet count monitoring to identify high-risk individuals. Thrombocytopenia consistently emerges as a more prevalent feature among dengue-positive

individuals compared to their dengue-negative counterparts. Moreover, the extent of thrombocytopenia during infections not only holds prognostic significance but also offers valuable insights aiding in differential diagnosis, presenting an avenue for discerning the severity and progression of dengue infections [46-48].

Amidst the complexities of dengue infection, the dynamics governing platelets encompass a nuanced interplay involving their destruction and suppression mechanisms. These processes, while not entirely elucidated, exhibit multifaceted pathways. Immune-mediated destruction emerges as a significant contributor: the dengue virus incites the production of antibodies targeting platelets, culminating in their clearance through immune complex activation of the complement system. Simultaneously, the virus directly infiltrates platelets, inducing dysfunction and subsequent elimination as it replicates within these blood components. Dengue infection extends its reach to the bone marrow, instigating suppression by infecting hematopoietic progenitor and stromal cells, thereby impeding platelet production. Concurrently, altered platelet function under the viral influence heightens their susceptibility to activation and aggregation, fostering microthrombi formation, and escalating platelet consumption, ultimately culminating in thrombocytopenia [49-52].

In the expansive realm of future directions in understanding platelet dynamics within dengue infection, numerous promising avenues beckon. Unraveling the intricate mechanisms triggering platelet activation during dengue stands as a pivotal quest, offering potential targets for therapeutic interventions. Equally compelling is the exploration into the role of platelets within the immune response, holding promise for novel immunomodulatory therapies and insights into viral clearance. Investigating platelet interactions with diverse immune cells, from monocytes to lymphocytes, carries the potential to shape strategies modulating these interactions for therapeutic ends. The quest for specific platelet biomarkers linked to disease severity opens vistas for early risk assessment and tailored clinical management. Uncharted territories encompass studies on platelet transfusion's role in severe dengue cases, promising evidence-based guidelines for optimized therapeutic interventions. Lastly, the horizon of platelet-targeted therapies, be it antiplatelet agents or tailored modulators, hints at transformative potential in mitigating disease severity, marking a frontier in therapeutic innovation for dengue management [38,46,53-55].

Conclusion

This research highlights the importance of platelet characteristics in the setting of dengue illness. A significant difference was seen in the severity of thrombocytopenia and the overall severity of the condition, as shown by a P-value of 0.013. The significance of platelet count in predicting the severity of Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS) is underscored by this observation. In addition, the research reveals a low Mean Platelet Volume (MPV < 9fl) and a large Platelet Distribution Width (PDW > 13fl) as indicators that have a heightened susceptibility for dengue fever. These indicators might serve as prognostic markers in places where the disease is common. Nevertheless, the research admits constraints, such as a limited sample size and a geographically confined focus. To strengthen these results, it is recommended that more studies be conducted in wider locations where the disease is often seen to confirm and extend the observed advantages to a more varied population.

References

1. Tuiskunen Bäck, A., & Lundkvist, Å. Dengue viruses – an overview. Infection Ecology & Epidemiology, 2013;3(1):19839.
2. Gubler, D. J. Dengue/dengue haemorrhagic fever: History and current status. In Novartis Foundation Symposia,2 006;277:3–22.
3. Khan, M. B., Yang, Z.-S., Lin, C.-Y., Hsu, M.-C., Urbina, A. N., Assavalapsakul, W., Wang, W.-H., Chen, Y.-H., & Wang, S.-F. Dengue overview: An updated systematic review. Journal of Infection and Public Health, 2023; 16(10):1625–1642.
4. Khetarpal, N., & Khanna, I. Dengue fever: Causes, complications, and vaccine strategies. Journal of Immunology Research, 2016:1–14.
5. da Silva-Voorham, J. M., Tami, A., Juliana, A. E., Rodenhuis-Zybert, I. A., Wilschut, J. C., & Smit, J. M. Dengue: a growing risk to travellers to tropical and sub-tropical regions. Nederlands Tijdschrift Voor Geneeskunde, 2009; 153.
6. Wilder-Smith, A., Murray, & Quam, M. Epidemiology of dengue: past, present and future prospects. Clinical Epidemiology, 2013; 5:299-309.
7. Tantawichien, T. Dengue fever and dengue haemorrhagic fever in adolescents and adults. Paediatrics and International Child Health, 2012; 32(sup1):22–27.
8. Sharma, S. N., Raina, V. K., & Kumar, A. Dengue/DHF: an emerging disease in India. The Journal of Communicable Diseases, 2000; 32(3):175-9.
9. Wu, T., Wu, Z., & Li, Y.-P. Dengue fever and dengue virus in the People's Republic of

China. Reviews in Medical Virology, 2022;32 (1):e2245.
10. Garmo, C., Bajwa, T., & Burns, B. Physiology, clotting mechanism, 2023.
11. Stassen, J., Arnout, J., & Deckmyn, H. The hemostatic system. Current Medicinal Chemistry,2004;11(17):2245–2260.
12. Doherty, T. M., & Kelley, A. Bleeding Disorders, 2023.
13. Khan, M. I., & Ullah, I. Diagnostic importance of mean platelet volume, platelet distribution width and platelet large cell ratio as screening tool in immune thrombocytopenia. Porto Biomedical Journal, 2020;5(6):e094.
14. Singh, A., & Varma, R. Role of platelet distribution width (PDW) and plateletcrit in the assessment of nonthrombocytopenic preeclampsia and eclampsia. Journal of Obstetrics and Gynaecology of India, 2018; 68(4):289–293.
15. Prasad, A., Saran, K., Vidya, K., Seema, K., & Prakash, J. Study of platelet indices and their role in evaluation of thrombocytopenia. Journal of Family Medicine and Primary Care, 2022;11(10):6236-6242.
16. Reddy, S. K. Significance of platelet volume indices in STEMI patients: A case-control study. Journal of Clinical and Diagnostic Research: JCDR, 2017;11(4):LC05-LC07.
17. Tozkoparan, E., Deniz, O., Ucar, E., Bilgic, H., & Ekiz, K. Changes in platelet count and indices in pulmonary tuberculosis. Clinical Chemistry and Laboratory Medicine, 2007;45 (8):1009-13.
18. Fan, Z., Pan, J., Zhang, Y., Wang, Z., Zhu, M., Yang, B., Shi, L., & Jing, H. Mean platelet volume and platelet distribution width as markers in the diagnosis of acute gangrenous appendicitis. Disease Markers, 2015:1–4.
19. Shilpi, K., & Potekar, R. M. A study of platelet indices in type 2 diabetes mellitus patients. Indian Journal of Hematology & Blood Transfusion: An Official Journal of Indian Society of Hematology and Blood Transfusion, 2018;34(1):115–120.
20. Pluta, M. P., Dziech, M., Klocek, T., Szczepańska, A. J., & Krzych, Ł. J. Diagnostic accuracy of platelet-derived parameters in prognostication in neurosurgery. International Journal of Environmental Research and Public Health, 2022;19(12):7115.
21. Kim, J. Y., Yoon, J., Lim, C. S., Choi, B. M., & Yoon, S.-Y. Clinical significance of platelet-associated hematological parameters as an early supplementary diagnostic tool for sepsis in thrombocytopenic very-low-birth-weight infants. Platelets, 2015;26(7):620–626.
22. Raju, K., Anand, A., & Azeem Mohiyuddin, S. M. Significance of platelet parameters in squamous cell carcinoma of oral cavity – A case-control study. Journal of Cancer Research and Therapeutics,2022;18(4):1036.
23. Hsieh, P.-Y., Hsu, K.-H., Chiang, M.-C., Hsu, J.-F., Chu, S.-M., & Lien, R. Platelet parameters and the association with morbidity and mortality in Preterm Infants. Pediatrics and Neonatology, 2023;64(1):68–74.
24. Beyan, C., Kaptan, K., & Ifran, A. Platelet count, mean platelet volume, platelet distribution width, and plateletcrit do not correlate with optical platelet aggegation responses in healthy volunteers. Journal of Thrombosis and Thrombolysis, 2006;22(3):16 1–164.
25. Matondang, A. V., Widodo, D., Zulkarnain, I., Rengganis, I., Trihandini, I., Inada, K., & Endo, S. The correlation between thrombopoietin and platelet count in adult dengue viral infection patients. Acta Medica Indonesiana, 2004;36(2):62-9.
26. Metri, B., & Jyothi, P. Correlation of serological markers and platelet count in the diagnosis of Dengue virus infection. Advanced Biomedical Research, 2015;4(1):26.
27. Oishi, K., Inoue, S., Cinco, M. T. D. D., Dimaano, E. M., Alera, M. T. P., Alfon, J. A. R., Abanes, F., Cruz, D. J. M., Matias, R. R., Matsuura, H., Hasebe, F., Tanimura, S., Kumatori, A., Morita, K., Natividad, F. F., & Nagatake, T. Correlation between increased platelet-associated IgG and thrombocytopenia in secondary dengue virus infections. Journal of Medical Virology, 2003;71(2):259–264.
28. Dadu, T., Sehgal, K., Joshi, M., & Khodaiji, S. Evaluation of the immature platelet fraction as an indicator of platelet recovery in dengue patients. International Journal of Laboratory Hematology, 2014;36(5):499–504.
29. Faridah IN, Dania H, Chen YH, Supadmi W, Purwanto BD, Heriyanto MJ, Aufa MA, Chang WC, Perwitasari DA. Dynamic Changes of Platelet and Factors Related Dengue Haemorrhagic Fever: A Retrospective Study in Indonesian. Diagnostics (Basel), 2022;12(4):95 0.
30. Bhattarai, B. R., Mishra, A., Aryal, S., Chhusyabaga, M., & Bhujel, R. Association of hematological and biochemical parameters with serological markers of acute dengue infection during the 2022 dengue outbreak in Nepal. Journal of Tropical Medicine, 2023:1–10.
31. Yasuda, I., Saito, N., Suzuki, M., Umipig, D. V., Solante, R. M., Guzman, F. D., Sayo, A. R., Yasunami, M., Koizumi, N., Kitashoji, E., Sakashita, K., Ng, C. F. S., Smith, C., & Ariyoshi, K. Unique characteristics of new complete blood count parameters, the Immature Platelet Fraction and the Immature

Platelet Fraction Count, in dengue patients. PloS One, 2021;16(11):e0258936.
32. Tsai, J.-J., Chang, J.-S., Chang, K., Chen, P.-C., Liu, L.-T., Ho, T.-C., Tan, S. S., Chien, Y.-W., Lo, Y.-C., & Perng, G. C. Transient monocytosis subjugates low platelet count in adult dengue patients. Biomedicine Hub, 2017; 2(1):1–16.
33. Ahmed, A. E., Dahman, B., Altamimi, A., McClish, D. K., & AL-Jahdali, H. The aspartate aminotransferase/platelet count ratio index as a marker of dengue virus infection: Course of illness. Journal of Infection and Public Health, 2020;13(7):980–984.
34. Metri, B., & Jyothi, P. Correlation of serological markers and platelet count in the diagnosis of Dengue virus infection. Advanced Biomedical Research, 2015;4(1):26.
35. Looi, K. W., Matsui, Y., Kono, M., Samudi, C., Kojima, N., Ong, J. X., Tan, C. A., Ang, C. S., Tan, P. H. Y., Shamnugam, H., Sekaran, S. D., Syed Omar, S. F., & Lum, L. C. S. Evaluation of immature platelet fraction as a marker of dengue fever progression. International Journal of Infectious Diseases: IJID: Official Publication of the International Society for Infectious Diseases, 2021;110:187–194.
36. Sharma, K. Association of mean platelet volume with severity, serology & treatment outcome in dengue fever: Prognostic utility. Journal of Clinical and Diagnostic Research: JCDR, 2015;9(11):EC01-3.
37. Metri, B., & Jyothi, P. Correlation of serological markers and platelet count in the diagnosis of Dengue virus infection. Advanced Biomedical Research,2015;4(1):26.
38. Shah, D., Khataniar, M., Sawhney, A., Nautiyal, M., Desai, R., & Kakar, A. An observational study to see the correlation between trends of platelet counts and immature platelet fraction in dengue infection. Tropical Doctor, 2021;51(3):378–381.
39. Jayanthi, H., & Tulasi, S. Correlation study between platelet count, leukocyte count, nonhemorrhagic complications, and duration of hospital stay in dengue fever with thrombocytopenia. Journal of Family Medicine and Primary Care, 2016;5(1):120-3.
40. Kulkarni, R. D., Patil, S. S., Ajantha, G. S., Upadhya, A. K., Kalabhavi, A. S., Shubhada, R. M., Shetty, P. C., & Jain, P. A. Association of platelet count and serological markers of dengue infection-importance of NS1 antigen. Indian Journal of Medical Microbiology, 2011;29(4):359–362.
41. Castilho, B. M., Silva, M. T., Freitas, A. R. R., Fulone, I., & Lopes, L. C. Factors associated with thrombocytopenia in patients with dengue fever: a retrospective cohort study. BMJ Open, 2020;10(9):e035120.
42. Hapsari Putri, I., Tunjungputri, R., De Groot, P., van der Ven, A., & de Mast, Q. Thrombocytopenia and platelet dysfunction in acute tropical infectious diseases. Seminars in Thrombosis and Hemostasis, 2018; 44(07): 683–690.
43. Vogt, M. B., Lahon, A., Arya, R. P., Spencer Clinton, J. L., & Rico-Hesse, R. Dengue viruses infect human megakaryocytes, with probable clinical consequences. PLoS Neglected Tropical Diseases, 2019;13(11):e00 07837.
44. Quirino-Teixeira, A. C., Andrade, F. B., Pinheiro, M. B. M., Rozini, S. V., & Hottz, E. D. Platelets in dengue infection: more than a numbers game. Platelets,2022;33(2):176–183.
45. Chakraborty, S., Alam, S., Sayem, M., Sanyal, M., Das, T., Saha, P., Sayem, M., Byapari, B. K., Tabassum, C. T., Kabir, A., Amin, M. R., & Nabi, A. H. M. N. Investigation of the efficacy and safety of eltrombopag to correct thrombocytopenia in moderate to severe dengue patients - a phase II randomized controlled clinical trial. E Clinical Medicine, 2020;29–30(100624):100624.
46. Lam, P. K., Van Ngoc, T., Thu Thuy, T. T., Hong Van, N. T., Nhu Thuy, T. T., Hoai Tam, D. T., Dung, N. M., Hanh Tien, N. T., Thanh Kieu, N. T., Simmons, C., Wills, B., & Wolbers, M. The value of daily platelet counts for predicting dengue shock syndrome: Results from a prospective observational study of 2301 Vietnamese children with dengue. PLoS Neglected Tropical Diseases, 2017;11(4):e000 5498.
47. Kulkarni, R. D., Patil, S. S., Ajantha, G. S., Upadhya, A. K., Kalabhavi, A. S., Shubhada, R. M., Shetty, P. C., & Jain, P. A. Association of platelet count and serological markers of dengue infection-importance of NS1 antigen. Indian Journal of Medical Microbiology, 2011;29(4):359–362.
48. Dhunputh, P., Acharya, R., Umakanth, S., Shetty, S. M., Mohammed, A. P., & Saraswat, P. P. Clinical profile of Thrombocytopenia in Acute Febrile Illnesses; a hospital-based study. Kathmandu University Medical Journal (KUM J), 2021;19(74):248-252.
49. Wan, S.-W., Lin, C.-F., Yeh, T.-M., Liu, C.-C., Liu, H.-S., Wang, S., Ling, P., Anderson, R., Lei, H.-Y., & Lin, Y.-S. Autoimmunity in dengue pathogenesis. Taiwan Yi Zhi [Journal of the Formosan Medical Association], 2013; 112(1):3–11.
50. Quirino-Teixeira, A. C., Andrade, F. B., Pinheiro, M. B. M., Rozini, S. V., & Hottz, E. D. Platelets in dengue infection: more than a numbers game. Platelets, 2022;33(2):176–183.

51. La Russa, V. F., & Innis, B. L. 11 Mechanisms of dengue virus-induced bone marrow suppression. Bailliere's Clinical Haematology, 1995;8(1):249–270.
52. Shahila M, A. G., & Jothilingam, P. A hospital based cross-sectional study on platelet parameters in adult patients with dengue, its serological subgroups, and controls. Platelets, 2022;33(2):291–297.
53. Losada, P. X., DeLaura, I., & Narváez, C. F. Dengue virus and platelets: From the biology to the clinic. Viral Immunology, 2022; 35(5): 349–358.
54. Wilder-Smith, A., Ooi, E.-E., Vasudevan, S. G., & Gubler, D. J. Update on dengue: Epidemiology, virus evolution, antiviral drugs, and vaccine development. Current Infectious Disease Reports, 2010;12(3):157–164.
55. Guo, L., & Rondina, M. T. The era of thrombo inflammation: Platelets are dynamic sensors and effector cells during infectious diseases. Frontiers in Immunology, 2019;10.