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CORRELATION BETWEEN ABDOMINAL ULTRASOUND FINDINGS AND PLATELET COUNT IN DENGUE FEVER PATIENTS: IMPLICATIONS FOR EARLY DIAGNOSIS AND MANAGEMENT

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Abstract

Objectives

This study aimed to investigate abdominal ultrasound changes in patients diagnosed with dengue fever and their relationship with platelet count.

Methods

A prospective observational study was conducted at a tertiary care medical college's radiology department in an urban area. One hundred cases diagnosed with dengue fever based on serology were included, following predefined inclusion and exclusion criteria.

Results

Among the 100 cases, 60 were male (60%) and 40 were female (40%). Seventy-six patients showed increased gallbladder wall thickness (GBWT) due to pericholecystic edema, 31 exhibited ascites, and 32 had splenomegaly. Thrombocytopenia was associated with increased third spacing and splenomegaly observed on abdominal ultrasound.

Practical Implications

This study emphasizes the importance of recognizing abdominal ultrasound features in suspected dengue cases while awaiting laboratory results. It provides crucial insights for medical professionals (undergraduates, postgraduates, and consultants) and patients, facilitating early intervention and potentially averting complications.

Conclusion

Gallbladder wall edema, splenomegaly, and ascites are prevalent in severe dengue cases. Detecting these features early may signal the likelihood of progression to severe dengue.

Keywords Dengue, Dengue shock syndrome, Dengue Hemorrhagic, Pericholecystic edema, Sonographic findings, Ascites, Splenomegaly, Pleural effusion.

INTRODUCTION

Dengue fever (DF) is a significant global health threat, primarily transmitted by the Aedes aegypti mosquito. This viral infection presents a myriad of symptoms, including sudden onset high-grade fever, anorexia, lethargy, headache, retro-orbital discomfort, myalgia, arthralgia, weakness, sore throat, and a macular skin rash. Severe cases of DF necessitate hospitalization, with an estimated 500,000 hospital admissions occurring annually worldwide (1-

2). The transmission of DF is facilitated by various factors, one of which is the structural similarity between the fatty acid synthase 1 (FAS1) of Aedes aegypti mosquitoes and that of humans. This

similarity potentially plays a crucial role in the viral replication process, contributing to the spread of the infection (3).

In Asian populations, DF exhibits a case-fatality rate ranging from 0.5% to 3.5% (4). Complications of DF extend beyond the typical flu-like symptoms and can affect multiple organ systems, including the hepatobiliary and vascular systems. Common hematological manifestations include bleeding diathesis and thrombocytopenia, which significantly impact disease severity (3, 5-6).

One severe complication of DF is Dengue Vascular Permeability Syndrome (DVPS), characterized by an increase in microvascular permeability. This

syndrome leads to plasma leakage, resulting in various clinical manifestations, including pleural effusion, ascites, gallbladder wall thickening (GBWT), hepatomegaly, and splenomegaly (3, 5, 7-8). Abdominal ultrasound has emerged as a valuable diagnostic tool in the assessment of DVPS-related changes. It offers a non-invasive method for detecting gallbladder wall thickening, ascites, and other signs of fluid accumulation, aiding in the early identification of patients at risk of progressing to the critical phase of the disease (7-9).

In comparison to traditional imaging modalities like chest X-rays, abdominal ultrasound demonstrates superior sensitivity in detecting pleural effusion, with the ability to detect smaller volumes of fluid. This heightened sensitivity enables early diagnosis and timely intervention, ultimately improving patient outcomes (10-11).

The primary objective of ongoing research in this field is to establish correlations between abdominal ultrasound findings, platelet counts, and disease severity in DF patients. By elucidating these relationships, clinicians aim to develop more effective strategies for early intervention and management, thereby reducing morbidity and mortality associated with severe DF cases.

METHODS

Data Collection

Following the Strobe guidelines, this prospective study was conducted at the Radiology department of Akhtar Saeed Trust Hospital. Over a one-month period from October 1st to October 30th, 2022, 100 patients diagnosed with dengue fever (confirmed via positive non-structural protein 1 (NS-1) antigen or elevated dengue immunoglobulin IgM) were included. Patients were referred from outpatient, inpatient, and emergency departments for abdominal ultrasonography. A 3.5 MHz curvilinear probe and water-soluble gel were utilized with a Toshiba Ultrasound machine for imaging. Scans were performed with patients in a supine position, employing the intercostal approach over the right hypochondrium region. Gallbladder wall thickness was measured using

calipers, with a normal upper limit set at 3 mm, measured on the anterior wall. Splenomegaly was defined as a spleen measuring more than 12 cm. Patients provided informed written consent via a questionnaire. The study protocol was approved by the institution's ethics committee.

Inclusion and Exclusion Criteria

Inclusion Criteria

1. Patients diagnosed with dengue fever based on serological tests, including positive results for non-structural protein 1 (NS-1) antigen or elevated dengue immunoglobulin IgM.

2. Patients who provided informed written consent to participate in the study.

3. Patients aged 18 years and above.

4. Dengue patients with a history of fever lasting fewer than 5 days.

Exclusion Criteria

1. Patients with pre-existing gallbladder disease were excluded from the study.

2. Individuals who declined to provide consent for participation.

3. Dengue patients with a history of fever lasting more than 5 days.

Search Strategy

To identify relevant literature on the diagnostic, prognostic, follow-up, and complication detection role of ultrasonography in dengue fever, comprehensive searches were conducted in standard medical electronic databases such as PUBMED and Google Scholar. The search terms 'dengue fever,' 'dengue hemorrhagic fever,' and 'dengue vascular permeability syndrome' were combined with terms such as 'ultrasound,' 'abdominal ultrasonography,' 'gall bladder thickening,' 'pericholecystic edema,' 'ascites,' and 'chest ultrasonography.' All types of studies including abstracts, case reports, case series, randomized controlled trials, non-randomized controlled trials, and comparative studies were retrieved and thoroughly reviewed. There were no restrictions imposed based on age, gender,

geographical location, or sample size."

Data Compilation and Statistical Analysis

The collected data were organized into tables using Microsoft Excel spreadsheet and analyzed utilizing SPSS 25.0 software. Statistical analysis was performed with a significance level set at $P \leq 0.05$.

RESULTS

Demographic Characteristics

In this cross-sectional study, 100 suspected cases of Dengue Fever (DF) underwent abdominal ultrasound examinations at the radiology department. Among them, 60 patients (60%) were male and 40 patients (40%) were female, all testing positive for dengue serology. Out of the 100 seropositive cases, patients were classified as 38 with DF without warning signs, 33 with DF exhibiting warning signs, and 29 with severe DF.

Correlation Analysis

Correlation analysis revealed significant associations between platelet count and both splenomegaly ($r = -0.371$, $p < 0.01$) (table 1), and ascites ($r = -0.643$, $p < 0.01$) (table 2), indicating that lower platelet counts were associated with a higher likelihood of these ultrasound findings.

Table 1: Correlation between Platelet Count and Splenomegaly. This table displays the Pearson correlation coefficients between platelet count and splenomegaly, along with their respective significance levels. The correlation coefficient of -0.371 indicates a significant negative correlation between platelet count and the presence of splenomegaly in patients with dengue fever. ** Correlation is significant at the 0.01 level (2-tailed).

		Platelet count	Splenomegaly
Platelet count	Pearson Correlation	1	-.371**
	Sig. (2-tailed)		.000
	N	100	99
Splenomegaly	Pearson Correlation	-.371**	1
	Sig. (2-tailed)	.000	
	N	99	99

Table 2: Correlation between Platelet Count and Ascites. This table presents the Pearson correlation coefficients between platelet count and ascites, along with their significance levels. The correlation coefficient of -0.643 suggests a significant negative correlation between platelet count and the occurrence of ascites in patients diagnosed with dengue fever. **. Correlation is significant at the 0.01 level (2-tailed).

		Platelet count	Ascites
Platelet count	Pearson correlation	1	-.643[**]
	Sig. (2-tailed)		.000
	N	100	100
Ascites	Pearson correlation	-.643[**]	1
	Sig. (2-tailed)	.000	
	N	100	100

Age Distribution

The age distribution analysis revealed that the most commonly affected age group among the studied cases was between 21 to 30 years, comprising 26% of the cases, followed by the age groups of 31 to 40 years (20%) and 41 to 50 years (13%). The mean age was 43.1 years with a standard deviation of 21.02 (Fig 1)
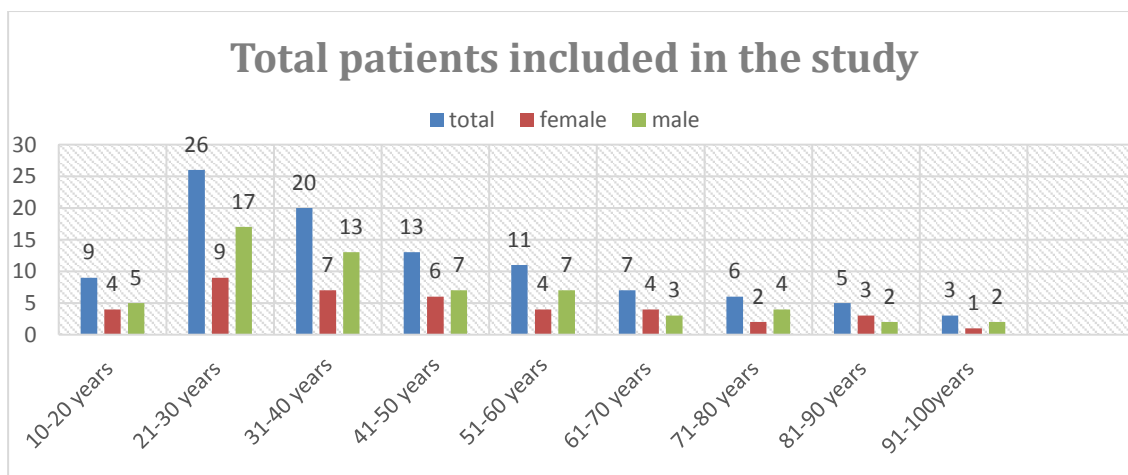
Figure 1: Age Distribution of Dengue Fever Cases.

This figure illustrates the distribution of age groups among patients diagnosed with dengue fever. The most commonly affected age group was 21 to 30 years, representing 26% of the cases. Subsequently, the age groups of 31 to 40 years and 41 to 50 years accounted for 20% and 13% of the cases, respectively.

Presenting Complaints

High-grade fever was the predominant presenting complaint among all patients (100%). Additional complaints included nausea, vomiting, fatigue, sore throat, dry cough, epigastric pain, myalgia, arthralgia, severe headache, and retro-orbital pain.

Sonographic Findings

On the day of presentation, Gallbladder Wall Thickness (GBWT) and Pericholecystic edema, indicated by an increase in gallbladder wall thickness, was observed in 76 out of 100 patients (76%). The mean thickness of pericholecystic edema was 6.25 mm, ranging from 3.7 to 11.3 mm. Mild to moderate ascites was detected in 31 out of 100 patients (31%). Splenomegaly, defined as a

spleen measuring more than 12 cm, was observed in 32 out of 100 patients (32%).

The mean thickness of pericholecystic edema in the study was 6.25 mm (range: 3.7 – 11.3 mm), higher than reported in another study by Nainggolan L et al (12). Abdominopelvic ascites was the least common finding, whereas in another study pleural effusion was reported as the least common finding (12).

A relationship between pericholecystic edema and platelet count was illustrated by a negative correlation in the scatter diagram (Fig 2)
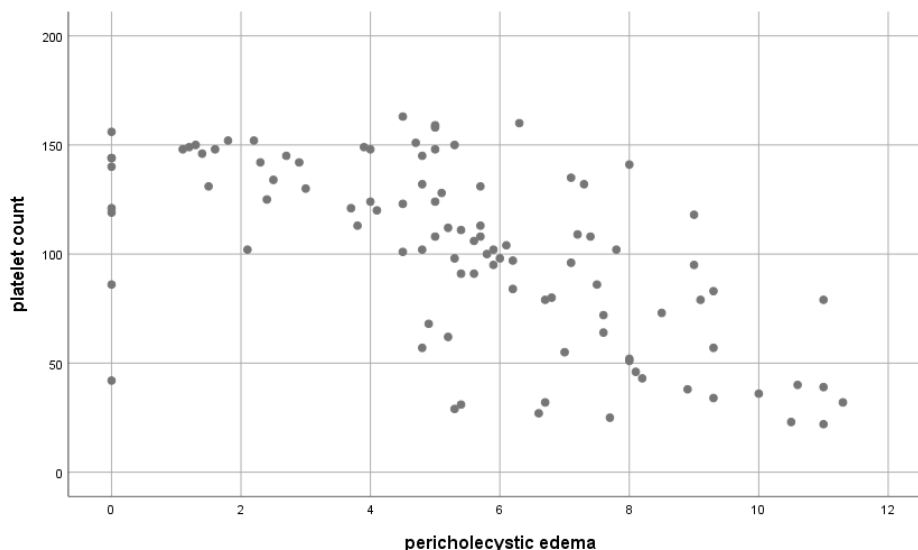

Fig 2: Scatter plot illustrating the relationship between pericholecystic edema (y-axis) and platelet count (x-axis) in patients with dengue fever.

Each data point represents an individual patient, with the negative correlation indicated by the downward trend of the dots.

The following figure shows the sonographic findings in different age groups. The X-axis shows the age and the y-axis shows the number of patients (Fig 3)
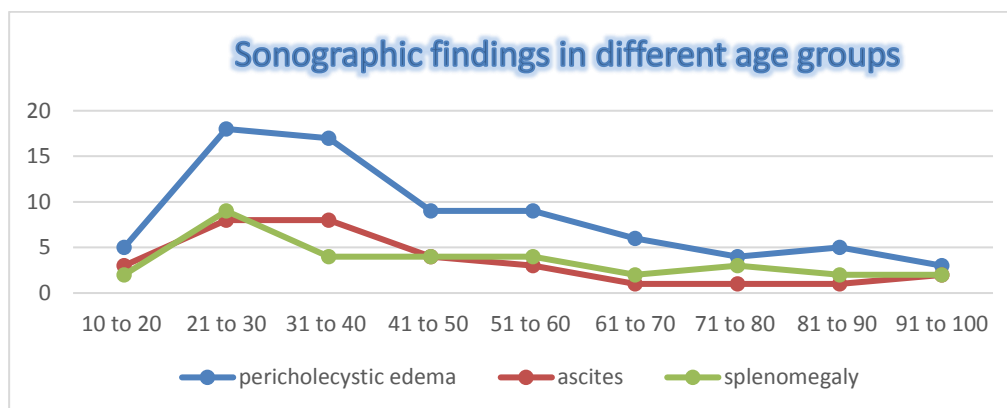
Figure 3: Sonographic Findings in Different Age Groups.

This figure displays the distribution of sonographic findings across different age groups of patients. The X-axis represents age groups, while the Y-axis indicates the number of patients.

Pericholecystic edema and ascites were more prevalent in patients with non-severe dengue with warning signs and severe dengue, with statistically significant differences noted (13). However, organomegaly incidence was comparable across different severity levels of dengue. Gall bladder wall thickness could not be measured in 8 patients due to contracted gall bladders.

Sonographic findings depicted in different patients illustrated various abnormalities, such as pericholecystic edema and pelvic free-fluid, indicative of plasma leakage into body cavities (Fig 4 and 5).

Fig. 4. A 31year old man presented to emergency with high-grade fever with chills, nausea, vomiting, arthralgias, and myalgias for 3 days.

CBC shows a platelet count of 75,000 and NS-1 came positive. The patient was sent for abdominal USG and pericholecystic edema of 9.8mm and mild pelvic ascites was seen. Just like ascites, pleural effusion is part of polyserositis which results in plasma leakage into the pleural cavity.

Fig. 5. Pelvic free-fluid seen in a 56-year-old woman with a history of 5-day fever and a platelet count of 43,000.

In a study by Kamrun Nahar, median platelet counts below specific thresholds were associated with various ultrasound findings, including gall bladder edema, ascites, pleural effusion, and hepatomegaly (14). The following table shows the relationship of platelet count with different ultrasonographic findings (table 3).

Table 3: Platelet count Relationship with pericholecystic edema, abdominopelvic ascites and splenomegaly

Platelet count	Pericholecystic edema	Abdominopelvic ascites	Splenomegaly
20,000-40,000	13	11	6
40,001-80,000	17	11	10
80,001-120,000	30	9	10
120,001-160,000	16	0	6

There was no mortality reported in our patients. We found a difference in the length of hospital stay, but this difference was not statistically significant. So therefore, when consolidated with clinical presentations of dengue patients, this finding may assist clinicians in further management of severe dengue

DISCUSSION

Infectious diseases continue to pose a significant global health challenge, with dengue fever standing out as one of the most prevalent and clinically diverse conditions (15-20). This cross-sectional study provides valuable insights into the clinical and sonographic characteristics of dengue fever (DF) patients undergoing abdominal ultrasound examinations. The predominance of males in our study population aligns with previous literature suggesting a higher susceptibility of males to dengue infection. The classification of patients into categories of DF severity—without warning signs, with warning signs, and severe DF—facilitates a comprehensive understanding of the disease spectrum (3-5, 21).

Gall bladder wall thickness (GBWT) or pericholecystic edema emerged as the most common sonographic finding in our study cohort, consistent with existing literature highlighting the utility of abdominal ultrasound in identifying plasma leakage manifestations characteristic of severe dengue (13). Interestingly, our study expands upon previous findings by Parmar JP et al., who identified four distinct GBWT patterns during their investigation into DF severity prediction. These patterns include a striated pattern of multiple hypoechoic layers separated by echogenic zones, an asymmetric pattern with echogenic tissue projecting into the gall bladder lumen, a central hypoechogenic zone separated by two echogenic layers, and a uniform echogenic pattern. Such detailed characterization of GBWT patterns enhances our understanding of the pathophysiological mechanisms underlying DF progression and may hold promise for refining prognostic algorithms (22).

The prevalence of mild to moderate ascites and organomegaly further underscores the systemic involvement of multiple organs during the course of dengue infection. Notably, the incidence of these sonographic findings demonstrated a negative correlation with platelet count, suggesting a potential association between disease severity and hematological parameters.

The age distribution analysis revealed a higher prevalence of DF among younger adults, particularly between the ages of 21 to 30 years, which may reflect increased exposure to mosquito vectors in this demographic group. The diverse array of presenting complaints underscores the multisystemic nature of DF, with high-grade fever being the hallmark symptom, consistent with the disease's acute febrile phase.

Comparisons with previous literature highlight variations in sonographic findings and their prevalence across different studies. While our study observed a higher mean thickness of pericholecystic edema compared to previous reports, the incidence of abdominopelvic ascites was relatively lower. Such differences underscore the heterogeneity of clinical presentations and sonographic manifestations in dengue patients, influenced by factors such as patient demographics, disease severity, and study methodologies (23-25).

Furthermore, the association between platelet count and ultrasonographic findings corroborates findings from previous studies, emphasizing the prognostic significance of hematological parameters in predicting disease progression and severity. The observed relationships between platelet count and sonographic abnormalities underscore the potential utility of ultrasound as a non-invasive tool for prognostication and risk stratification in dengue patients (26-27).

The clinical significance of our findings is underscored by their potential implications for patient management. While no mortality was reported in our study cohort, differences in hospital stay length were observed, albeit not statistically significant. Integrating sonographic findings with clinical presentations may aid clinicians in the timely identification of severe dengue cases, enabling prompt intervention and improved patient outcomes (28-29).

Overall, this study contributes to the existing body of literature on the clinical and sonographic characterization of dengue fever, emphasizing the importance of multimodal approaches for accurate diagnosis, prognostication, and management of this significant public health concern. Further longitudinal studies are warranted to validate the prognostic value of ultrasound findings and optimize their integration into clinical practice guidelines for dengue management.

LIMITATIONS

Follow-up ultrasound scans were not conducted after patients were discharged from the hospital.

CONCLUSION

Ultrasound serves as a valuable adjunctive tool for detecting fluid leakage and plays a crucial role in cost-effective prediction of disease severity. The observed findings, such as gallbladder wall thickening, pleural effusion (bilateral or unilateral), ascites, and splenomegaly, strongly support the diagnosis of dengue fever and aid in achieving an early diagnosis. These abdominal findings, combined with the gradual decrease in platelet count, indicate the severity of the illness and influence disease prognosis.

Availability of data and materials

All data and materials are retained by the first and corresponding authors.

Conflict of interest

The authors declare no conflicts of interest.

REFERENCES

1. Guzman MG, Gubler DJ, Izquierdo A, Martinez E, Halstead SB. Dengue infection. Nat Rev Dis Primers. 2016 Jul 21;2:16055. doi: 10.1038/nrdp.2016.55

2. World Health Organization. Dengue and severe dengue. Available at: https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue. Accessed January 2022.

3. Moras E, Achappa B, Murlimanju BV, Raj GN, Holla R, Madi D, D'Souza NV, Mahalingam S. Early diagnostic markers in predicting the

severity of dengue disease. 3 Biotech. 2022 Oct;12(10):268. doi: 10.1007/s13205-022-03365-3.

4. Nguyen TT, Le NT, Nguyen NM, Do VC, Trinh TH, Vo LT. Clinical features and management of children with dengue-associated obstructive shock syndrome: A case report. Medicine (Baltimore). 2022 Oct 28;101(43):e31322. doi: 10.1097/MD.0000000000031322. PMID: 36316901; PMCID: PMC9622697.

5. Manzoor N, Farooq SM, tul Sughra SK, Siddiqi MI, Arooj S, Ishfaq A, Gilani SA, ul Abidin SZ. Role of ultrasonography in the diagnosis of dengue fever: Ultrasonography in The Diagnosis of Dengue Fever. Pakistan BioMedical Journal. 2022 Jan 31:375-9.

6. Santhosh VR, Patil PG, Srinath MG, Kumar A, Jain A, Archana M. Sonography in the diagnosis and assessment of dengue Fever. J Clin Imaging Sci. 2014 Mar 21;4:14. doi: 10.4103/2156-7514.129260. PMID: 24744971; PMCID: PMC3988603.

7. Thomas L, et al. Dengue Vascular Leakage Is Augmented by Mast Cell Degranulation Mediated by Immunoglobulin Fcγ Receptors. eLife. 2016;5:e05291. doi: 10.7554/eLife.05291.

8. Ibrahim MA, Hamzah SS, Md Noor J, et al. The association of ultrasound assessment of gallbladder wall thickness with dengue fever severity. Ultrasound J. 2022;14:13. doi: 10.1186/s13089-022-00262-w.

9. Leite LA, Macedo FC. Abdominal ultrasound findings in patients with dengue fever. J Diagn Med Sonogr. 2019;35(4):291-296.

10. Dewan N, Zuluaga D, Osorio L, Krienke ME, Bakker C, Kirsch J. Ultrasound in Dengue: A Scoping Review. Am J Trop Med Hyg. 2021 Jan 18;104(3):826-835. doi: 10.4269/ajtmh.20-0103. PMID: 33534759; PMCID: PMC7941833.

11. Moro L, et al. Comparison between chest X-ray and ultrasound diagnosis of pulmonary complications in patients with severe dengue. Rev Soc Bras Med Trop. 2017;50(3):353-356.

12. 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

13. Martínez-Sellés M, et al. Cardiac findings in patients with dengue fever epidemic. Rev Esp Cardiol (Engl Ed). 2015;68(11):991-992.

14. Nahar K, Akhter S, Barua S, Begum D, Hasan MK. Ultrasonographic assessment of dengue fever and its correlation with platelet count: Correlating USG and platelet count in dengue fever. Bangladesh Med Res Counc Bull. 2021;47(1):23-8.

15. Azhar A, Saeed U, Piracha ZZ, Amjad A, Ahmed A, Batool SI, et al. SARS-CoV-2 related HIV, HBV, RSV, VZV, Enteric viruses, Influenza, DENV, S. aureus and TB co-infections. Arch Pathol Clin Res. 2021;5(1):026-033.

16. Piracha ZZ, Saeed U, Ahmed RAI, Khan FNA, Nasir MI. Global emergence of Langya virus: A serious public health concern. J Global Health. 2023;13.

17. Piracha ZZ, Saeed U, Tariq MN, Gilani SS, Rauf M, Ghyas H, et al. Emerging One Health Preparedness to Combat National Burden of Diseases in Pakistan: A Comprehensive Insight. J Community Med Health Solutions. 2023;4(2):080-088.

18. Piracha ZZ, Tariq MN, Rasool M, Gilani SS, Saeed U, Rana MSF, Arif M, et al. Catalyzing Global Action: Addressing SARS-CoV-2 Vaccine Hesitancy, Knowledge Disparities, and Epidemic Preparedness Challenges in Pakistan. Biomed J Sci & Tech Res. 2022;52(3):43702-43707.

19. Uppal SR, Uppal R, Khan AA, Saeed U, Piracha ZZ, Ali Z. Estimating the Prevalence of Fungal Nail Infections and Potential Concerns for Central Disease Surveillance Hub in Pakistan. Arch Clin Biomed Res. 2022;6(3):462-465.

20. Uppal SR, Khan AA, Uppal R, Saeed U, Piracha ZZ, Uppal R. Rising Surge of Antimicrobial Resistance and Urinary Tract Infections in

Pakistani Children: A Potential Life-Threatening Scenario. Fortune J Health Sci. 2022;5(2):281-283.

21. Araújo FMM, et al. Sonographic findings in patients with dengue fever. J Ultrasound Med. 2019;38(2):491-497.

22. Parmar JP, Mohan C, Vora M. Patterns of Gall Bladder Wall Thickening in Dengue Fever: A Mirror of the Severity of Disease. Ultrasound Int Open. 2017 Apr;3(2):E76-E81. doi: 10.1055/s-0043-105262. Epub 2017 Jun 7. PMID: 28603785; PMCID: PMC5464115.

23. Tandon R, Yadav D. Ultrasonographic findings in dengue hemorrhagic fever: a retrospective analysis. J Clin Diagn Res. 2016;10(6):TC10–TC13. doi: 10.7860/JCDR/2016/18114.7990.

24. Guzmán MG, Harris E. Dengue. Lancet. 2015;385(9966):453-465. doi: 10.1016/S0140-6736(15)00126-8.

25. Huy NT, et al. Factors associated with dengue shock syndrome: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2015;9(6):e0003972. doi: 10.1371/journal.pntd.0003972.

26. Tan J, Liu J, Zhang Q. The relationship between platelet count and ultrasonographic findings in patients with dengue fever: A retrospective analysis. Medicine (Baltimore). 2018;97(51):e13727. doi: 10.1097/MD.0000000000013727.

27. Kalayanarooj S, et al. Platelet-associated dengue illness (PADI): a novel risk factor for dengue hemorrhagic fever. Pathog Glob Health. 2017;111(7):332-341. doi: 10.1080/20477724.2017.1392423.

28. Lye DC, et al. The first dengue epidemic in Singapore: a cost analysis. Trans R Soc Trop Med Hyg. 2014;108(5):305-312. doi: 10.1093/trstmh/tru059.

29. Thomas L, et al. Evaluation of a commercial dengue NS1 antigen-capture ELISA for laboratory diagnosis of acute dengue virus infection. J Virol Methods. 2009;15(2):151-154. doi: 10.1016/j.jviromet.2009.03.024