

Clinical Significance of Ultrasonographic Findings in Dengue Patients; The Comparison of 2019 and 2022 Out Breaks

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ABSTRACT

Objective: To signify the ultrasonographic findings as an adjunct to serological diagnosis of dengue fever and to correlate ultrasound findings of dengue patients from the disease outbreak in 2019 and 2022 Pakistan with serological parameters such as platelet count, WBC and hematocrit.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Radiology Department, Federal Government Polyclinic (PGMI), Islamabad, Pakistan from Jan 2019 to Dec 2022.

Methodology: All patients referred to the Radiology Department for an Ultrasound Abdomen, who were admitted to the Hospital Isolation Unit and were found to have anti-dengue serology, were included in the data. Ultrasonographic findings of dengue patients from the disease outbreak in 2019 and 2022 along with serological parameters such as platelet count, WBC and Hematocrit were assessed.

Results: Out of 343 diagnosed dengue fever patients from the 2019 and 2022 outbreaks Pakistan, the majority (n=176; 51.3%) patients had thickening of the gall bladder wall finding, followed by hepatomegaly (n=100; 29.2%), ascites (n=94;27.4%), pleural effusion (n=84; 24.5%), splenomegaly (n=47; 13.7%) and perinephric fluid (n=8;2.3%). Thickness of the gallbladder (n=90; 68.2%) wall was most common in cases with platelet counts <40,000. There was a statistically significant difference found with reduced platelet count and gall bladder wall thickening (p -value < 0.001), pleural effusion (p -value=0.008) and ascites (p -value < 0.001). In 2019, Dengue fever was more severe than in 2022 in patients.

Conclusion: The ultrasonographic findings and their co-relation with serological parameters identify USG as a competitive diagnostic procedure for dengue fever.

Keywords: Dengue fever, Serology, Thrombocytopenia, Ultrasonography.

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INTRODUCTION

An estimated 100 million dengue cases are reported annually worldwide, with more than 80% of these illnesses being mild or asymptomatic. The majority of infections occur in Southeast Asia.^{1,2} Three million three hundred thirty-three thousand two hundred fifty-one dengue cases had been registered as of October 27, 2022, and 2,984 people had passed away globally.^{3,4} According to the World Health Organization (WHO), dengue fever was first identified in Pakistan in 1994, and since then, there have been more laboratory-confirmed cases.^{2,5,6} The country reported the greatest incidence of dengue in some of the explosive epidemics in 2011, 2013, 2015, 2017, 2019 and 2022 due to climate factors, an overcrowded population, and a lack of effective vector control methods.^{7,8} Dengue cases are occasionally seen throughout the year, although the monsoon season, which lasts from July to September, has the highest incidence. Punjab,

Khyber Pakhtunkhwa, & Sindh were the most severely impacted provinces during the dengue outbreak recorded in 2022 during the post-monsoon season from August to October.⁹

Timely identification of plasma leakage and dengue hemorrhagic fever (DHF) is crucial for managing the disease effectively. In the early stages, ascites and effusion may not be easily diagnosed through simple radiology and clinical examination.¹⁰ However, ultrasonography is a reliable method for detecting even minimal amounts of ascites and effusion at any stage of the disease, aiding in early diagnosis of DHF. The objective of this study was to signify the ultrasonographic findings as an adjunct to serological diagnosis of dengue fever and correlate ultrasound findings of dengue patients from the disease outbreak in 2019 and 2022 in Pakistan with serological parameters of platelet count, WBC and Hematocrit.

METHODOLOGY

The prospective longitudinal study was conducted at the Radiology Department of Federal

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Government Polyclinic (PGMI), Islamabad, Pakistan by utilising the radiological data available of diagnosed dengue patients from 2019 and 2022 outbreaks at the data repository of Federal Government Polyclinic Hospital, FGPC (PGMI), Islamabad Pakistan. The study has been approved by the Ethical Committee of Federal Government Polyclinic, Islamabad (Dated March 23 2023).

Inclusion Criteria: All patients referred to the Radiology department for Ultrasound Abdomen, who were admitted to the Hospital Isolation Unit and were found to have anti-dengue serology, were included.

Exclusion Criteria: Patients who had contracted dengue but had myeloproliferative, lymph-proliferative, thalassemia, or aplastic anaemia were not included.

Any suspected case of dengue that was reported to the Hospital Emergency Room by a consulting doctor and had either serological evidence of positive nonstructural protein 1 (NS-1) antigen or raised dengue immunoglobulin IgM, if both are negative, and the patient had a four-fold or higher rise in the paired dengue specific IgG immunoglobulin, was defined as a confirmed case of the disease. These included the patients referred from the Medical Emergency and OPD with the clinical and serological diagnosis of dengue fever and outside referrals.

Informed consent was obtained from the patient. All the demographic features of patients were recorded. Ultrasound of the abdomen was performed by a single operator, a Consultant Radiologist, on a Toshiba/Canon Xario 100 machine using a 3.75 MHz curved-array transducer. The patient was examined in supine, right, and left lateral decubitus positions. A general survey of the abdomen was done to find the presence of gall bladder wall thickening, hepatomegaly, splenomegaly, perinephric fluid, pleural effusions, ascites or hepatic parenchymal changes. Splenomegaly and hepatomegaly had cut-off measurements of 12cm and 15cm, respectively. Both ultrasound and laboratory tests were conducted free of cost.

The Statistical Package for the Social Sciences (SPSS) version 23:00 was used for data analysis. Kolmogorov-Smirnov test and the Shapiro-Wilk test were applied to check the normality of the data. Median and IQR were calculated for quantitative variables as the data deviated from the normal distribution. At the same time, frequency and percentage were calculated for qualitative variables. The ultrasound findings of the 2019 dengue and 2022 outbreak patients were compared with the help of the chi-square test. The *p*-value of ≤ 0.05 was rendered significant.

RESULTS

Three hundred forty-three patients were enrolled in the study; the median age was 30 (43-21), ranging from 5 to 92 years. Of 246(71.7%) were male and 97(28.3%) were females. Of 97 females, 39(40.2%) were not adults; out of 58 adult females, 27(46.5%) were pregnant. All patients had positive NS1 antigen test (nonstructural protein 1). IGM was performed on 16 patients; out of 16 patients, 14 patients had positive IGM, and only two patients had both positive IGM and positive IGg. The median of WBC, Hematocrit and Platelets was 4000 cells/ mL (5700 - 3000 cells / mL), 42 (45-37.60) and 51000 platelets/microL (81000-28000/microL), respectively. The majority (n=176; 51.3%) patients had thickening of the gall bladder wall finding, followed by hepatomegaly (n=100; 29.2%), ascites (n=94;27.4%), pleural effusion (n=84; 24.5%), splenomegaly (n=47; 13.7%) and perinephric fluid (n=8;2.3%) shown in Table-I.

Table-I: Frequency of different Ultrasonographic Findings in Dengue fever (n=343)

Ultrasonographic Features	Frequency (%)
Gall bladder wall thickening	176(51.3%)
Pleural effusion	84(24.5%)
Ascites	94(27.4%)
Hepatomegaly	100(29.2%)
Splenomegaly	47(13.7%)
Perinephric fluid	8(2.3%)

In Table-II, we correlated the ultra-sonographic findings with platelet count. The thickness of the

Table-II: Comparison of Ultrasonographic findings with Platelet Count (platelets/ microLitre) in Dengue fever (n=343)

Ultrasonographic Features	< 40,000 (n=132)	40,000 - 80,000 (n=123)	81,000 to 150,000 (n=64)	>150,000 (n=24)	<i>p</i> -value
Gall bladder Wall Thickening	90(68.2%)	60(48.8%)	18(28.1%)	8(33.3%)	<0.001
Pleural Effusion	46(34.8%)	25(20.3%)	8(12.5%)	5(20.8%)	0.008
Ascites	54(40.9%)	29(23.6%)	8(12.5%)	3(12.5%)	<0.001
Hepatomegaly	39(29.5%)	38(30.9%)	15(23.4%)	8(33.3%)	0.684
Splenomegaly	18(13.6%)	20(16.3%)	7(10.9%)	2(8.3%)	0.753
Perinephric Fluid	4(3.0%)	2(1.6%)	2(3.1%)	0	0.837

gallbladder (n=90; 68.2%) wall was the most common finding in cases with platelet counts <40,000/ microL and Perinephric fluid was the least common finding (n=4, 3.0%) with platelet counts <40,000/microL. There was a statistically significant difference found with reduced platelet count and gall bladder wall thickening (*p*-value <0.001), pleural effusion (*p*-value= 0.008) and ascites (*p*-value <0.001). Thickness of the gallbladder wall 110(53.9%), hepatomegaly (n=63; 30.9%), Ascites (n=59; 28.9%), Pleural effusion (n=46; 22.5%), Perinephric fluid (n=5;2.5%) were most common in cases <4,500/ mL WBC count. 27.3% cases of Pleural effusion and Hepatomegaly had 4,500–11,000 / mL WBC count. Table-III shows no statistical difference between sonographic findings with WBC in Dengue fever (*p*-value>0.05). When we correlated the Ultra sonographic findings with Hematocrit, only Hepatomegaly had a statistically significant difference with Hematocrit as *p*-value=0.040, as shown in Table-IV. In 2019, Dengue fever was more severe than in 2022 in patients. All the patients in our study completely recovered in 2022, & only one died in 2019. The clinical and sonographic findings are shown in Table-V.

Table-III: Comparison of Ultrasonographic findings with WBC (cells/mL) in Dengue fever (n=343)

Ultrasonographic Features	<4,500 (n=201)	4,500-11,000 (n=132)	>11,000 (n=6)	<i>p</i> -value
Gall bladder wall thickening	110(53.9%)	64(48.5%)	2(33.3%)	0.594
Pleural effusion	46(22.5%)	36(27.3%)	1(16.7%)	0.725
Ascites	59(28.9%)	32(24.2%)	2(33.3%)	0.605
Hepatomegaly	63(30.9%)	36(27.3%)	1(16.7%)	0.670
Splenomegaly	32(15.7%)	14(10.6%)	1(16.7%)	0.393
Perinephric fluid	5(2.5%)	3(2.3%)	0(0%)	0.800

Table-IV: Comparison of Ultrasonographic Findings with Hematocrit in Dengue Fever (n=343)

Ultrasonographic Features	<36 (n=61)	36-50 (n=265)	>50 (n=17)	<i>p</i> -value
Gall bladder wall thickening	28(45.9%)	139(52.5%)	9(52.9%)	0.148
Pleural effusion	12(19.7%)	69(26.0%)	3(17.6%)	0.645
Ascites	16(26.2%)	74(27.9%)	4(23.5%)	0.629
Hepatomegaly	23(37.7%)	68(25.7%)	9(52.9%)	0.040
Splenomegaly	8(13.1%)	35(13.2%)	4(23.5%)	0.586
Perinephric fluid	2 (3.3%)	5(1.9%)	1(5.9%)	0.308

DISCUSSION

The frequency of dengue fever has increased recently because of unchecked urbanisation, which has led to uncontrolled infrastructural development and a lack of sanitary utilities, creating an excess of mosquito breeding grounds.¹¹⁻¹³ Although the first dengue

outbreak from Pakistan was reported in 1994, it was in November 2005 that Karachi started to experience an annual epidemic pattern. Since then, dengue fever outbreaks have spread sporadically in Pakistan, eventually becoming severe epidemics in 2011, 2017, 2018, and 2019.¹⁴ According to data from the National Institute of Health, Pakistan reported 75,450 dengue cases from January to November 2022. The majority of these cases were reported from Khyber Pakhtunkhwa (n=22,617), Sindh (n=22,174), Punjab (n=18,626), Islamabad (n=5384), Balochistan (n=5205), and Azad Jammu and Kashmir (n=1444). Additionally, 136 fatalities (61 in Sindh, 45 in Punjab, 18 in KP, 11 in Islamabad, and 1 in Balochistan) had been reported. Heavy rains in Pakistan that resulted in devastating floods that displaced many people and provided mosquito breeding grounds are a major factor in the rise in dengue infections during 2022.^{8,9}

Table-V: Comparison of 2019 And 2022 Outbreak of Dengue Fever

Features	2019	2022
Gall Bladder Wall Thickening (N=176)		
Mild	36(20.4%)	51(28.9%)
Moderate	55(31.3%)	34(19.4%)
Pleural effusion (n=84)	44(52.3%)	40(47.7%)
Ascites (n=94)	53(56.4%)	41(43.6%)
Hepatomegaly (n=100)	55(55.0%)	45(45.0%)
Splenomegaly (n=47)	26(55.3%)	21(44.7%)
Perinephric fluid (n=8)	8(100.0%)	0(0%)
Platelet Count (Platelets / Microl)		
<40,000 (n=132)	59(44.7%)	73(55.3%)
40,000-80,000 (n=123)	58(47.1%)	65(52.9%)
81,000-150,000 (n=64)	20(31.3%)	44(68.7%)
>150,000 (n=24)	9(37.5%)	15(62.5%)
WBC (Cells/mL)		
<4,500 (n=204)	86(42.2%)	118(57.8%)
4,500-11,000 (n=132)	58(43.9%)	74(56.1%)
>11,000 (n=7)	2(28.6%)	5(71.4%)
Hematocrit		
<36 (n=61)	17(27.8%)	44(72.2%)
36-50 (n=265)	124(46.8%)	141(53.2%)
>50 (n=17)	5(29.4%)	12(70.6%)
Death (n=1)	1(100.0%)	0 (0%)

The results of our study have shown gall bladder wall thickening (51%), hepatomegaly (29.2%) and ascites (27.4%) as few of the major sonographic findings in the dengue patients. splenomegaly (1.3%), ascites (29.4%) and hepatomegaly (7.4%) have been similarly reported as common findings among patients of a study conducted in Bangladesh by Mehmood *et al.*¹⁵

Hepatomegaly and splenomegaly made up 28.4% of the total in a study by Zeb *et al.* while ascites made

up 23.5%, pleural effusion made up 7.1%, and gallbladder thickness made up 7.1% of the patients with a confirmed diagnosis of dengue fever. A significant *p*-value of 0.05 was established when all of these ultrasonography results were related to the dengue's severity as measured by the decline in platelet count (<40,000/microL).¹⁶ Similar findings were also reported in our research.

In a different study, around 67% of patients had thickened gallbladder (GB) walls due to oedema, 64.5% had ascites, 50% had pleural effusions, 17.7% had hepatomegaly, and 16.7% had splenomegaly. The most frequent findings in all age categories were edematous GB wall thickening, ascites, and pleural effusion. Patients with <40,000 platelets were likelier to have ascites, pleural effusion, and thickened, edematous GB walls.¹⁷ Our study supports these results.

In their investigation of dengue patients, Balasubramanian *et al.* analysed radiographic and ultrasonographic data concerning hematocrit. Around 91% of patients had plasma leakage that was detected on ultrasonography. Ultrasonography and the area-specific (liver) hematocrit were both sensitive for detecting and excluding plasma leakage for dengue detection.¹⁸ A study conducted by Parmar *et al* showed significant ultrasound changes in Gall gallbladder wall thickensening (GBWT) in admitted dengue patients, which is concurrent with the results of this study.¹⁹

Ultrasonographic findings compete to be one of the most reliable methods of diagnosis and severity of dengue fever, along with serological measures in the patients.²⁰ In patients presenting with fever and concurrent symptoms, especially during an epidemic, sonographic signs of thickening GB wall, pleural effusion (bilateral or right side), ascites, hepatomegaly, and splenomegaly should strongly favour the diagnosis of dengue fever. WBC count does not statistically account for any relationship with ultra-sonographic findings of dengue patients. In contrast, lower platelet count can be predicted if most of the ultrasonographic complications are present in a suspected case of dengue fever. This has been shown consistently in our study during the outbreaks of both 2019 and 2022.

CONCLUSION

The ultrasonographic findings and their co-relation with serological parameters identify USG as a competitive diagnostic procedure for dengue fever.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MB & SS: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

AR & SID: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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