ORIGINAL ARTICLE

Role of Sonography in the Assessment of Dengue Fever with Serological Correlation

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ABSTRACT

Objective: To assess ultrasound findings and their correlation with hematological parameters in patients with serologically confirmed Dengue Fever (DF).

Study Design: Cross-sectional study.

Place and Duration of Study: The study was carried out at the Department of Medicine of Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan from April 2022 to July 2022.

Methods: All participants in this study were serologically confirmed to have dengue disease. Each participant underwent chest, abdomen, and pelvis ultrasound examinations and a complete blood count (CBC). Both descriptive and analytic factors were analyzed statistically. Chi-Square / Fisher exact tests were employed to determine the connection between variables. A *p*-value less than (0.05) was statistically significant.

Results: 166 individuals with Dengue NS-1 antigen positive with a mean age of 35.77±11.13 years were included in this research. The mean duration of symptoms at the time of admission was 7.32± 1.86 days, and the average duration of hospital stay was 6.69± 2.01 days. Edema of the gallbladder wall was noticed in 67 (40.36%) of patients, whereas hepatomegaly was observed in 82 (49.39%). Ascites in 49 (29.51%), Pleural effusion in 48 (28.91%), and splenomegaly in 37 (22.28%). The average count of megakaryocytes was 97.09± 43.10. Significantly more sonographic anomalies were identified in patients younger than 36 years of age.

Conclusion: Ultrasound helps in early detection of leaky phase and complications in serologically confirmed patients with Dengue Fever who need prompt medical care.

Keywords: *Leaky Phase, NS-1 Antigen, Sonography, Thrombocytopenia, Viral Infection*.

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Introduction

Dengue virus infections occur in 390 million individuals annually.[1] Dengue fever (DF) is now endemic all over the globe and Asia shares almost 70% of the disease burden alone. In Pakistan, the first case of dengue fever was reported in 1994, and the incidence is progressively increasing ever since.[2] In year 2022, around 25932 individuals were diagnosed with dengue fever and mortality was reported in 62 (0.25%) cases.[3] This viral illness has imposed a great financial strain throughout the whole world, being more troublesome for resource-constrained countries like Pakistan. It is also a major concern in health departments around the world. Mosquitoes belonging to families Aedes aegypti and albopictus as vectors of the disease, dengue virus infection can simply present as DF or as more severe forms including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[4]

Patients with dengue virus infection could pass through different clinical phases, of which the leaky phase is the most critical one.[5] During this part of the illness, patients frequently develop third spacing and thus become more prone to complications, including death. It is therefore important to pick this stage at the earliest to prevent excessive morbidity and mortality. It is well known that ultrasound is more

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sensitive than clinical signs in eliciting smaller pleural effusions and ascites and could thus be handy in quicker recognition of leaky phase.[6] DHF complications can be picked up easily with the help of ultrasound. It is an effective diagnostic modality along with other hematological investigations in diagnosing and predicting disease severity. Plasma leakage in the form of fluid in the abdominal and pleural cavity helps in timely management.[7] According to the study published in BMC infectious diseases timely detection of pleural effusion in patients with DF helps in the assessment of disease severity, fluid management, and prediction of disease progression.[8]

Abnormalities in blood counts are also frequent among patients with dengue fever. Complete blood counts are checked in all patients with suspected or confirmed dengue virus infection at admission and are repeated frequently in a vast majority. Abnormalities in these cell lines have been shown to be associated with poor clinical outcomes previously. We postulated that these abnormalities at the time of admission could be used to predict ultrasound abnormalities in our patients. We, therefore, planned this study to determine the frequency of ultrasonographic abnormalities in hospitalized patients with dengue virus infection and to study their relationship with abnormalities in different hematological cell lines. The results would help us identify patients having a tendency towards developing more severe forms of the disease during hospital stay. Such patients could then benefit from more personalized aggressive treatment strategies.

Methods

This Cross sectional study was carried out in the Department of Medicine of Pak Emirates Military Hospital (PEMH), Rawalpindi, Pakistan from April 2022 to July 2022. The protocol for this was approved by ethical review committee of the institute vide letter number A/28/166(1)/EC/453/2022 held on May 02, 2022. The sample size was calculated with the help of the WHO sample size calculator with 95% confidence interval with a prevalence of DF 13% among the Pakistani population and convenience sampling technique was used for sampling. Dengue fever was diagnosed on the basis of a positive test for Dengue NS-1 antigen or IgM antibodies against dengue virus. All such patients who gave consent were included in this study. Patients with similar clinical presentation but negative Dengue NS-1 antigen/ IgM antibodies or those treated as outpatients were excluded. Basic demographic data and clinical details were recorded for all the patients at the time of admission. At the same time, complete blood counts were checked using the Sysmex Hematology Analyzer. Free of cost Ultrasound abdomen and chest were performed in patients with abnormal physical and laboratory parameters to confirm the leaky phase and to look for various abnormalities, including the presence of hepatomegaly, splenomegaly, gall bladder thickness, ascites, and pleural effusion, and to initiate aggressive management to prevent further complications.

We used SPSS 23 for data analysis. For this purpose, we divided the patients into two groups: 'younger patients' aged less than 36 years and 'older patients' aged 36 years or more. Quantitative variables were described as mean± standard deviation or proportions. Continuous variables were compared amongst different groups using independent samples t-test. Comparison of proportions amongst other groups was made using chi-square test or Fischer's exact test (for small sized samples having values of less than five in any of the cells of 2x 2 table). *P* values ≤0.05 were considered significant.

Results

This study was done on 166 patients with an average age of 35.77 ± 11.13 years. Out of these, 145 (87.3%) were males and 21(12.6%) were females. There were 86 patients younger than 36 years, and 80 patients aged 36 years or older. The mean duration of symptoms at the time of admission was 7.32± 1.86 days, and the average duration of hospital stay was 6.69± 2.01 days. A comparison of different hematological and ultra-sonographic features amongst younger and older patients is shown in Table 1.

Hepatomegaly and unilateral pleural effusion were more common among the younger patients. Patients with a lower platelet count had a longer duration of hospital stay, as well as the occurrence of various ultrasonographic abnormalities. However, this was not valid for abnormalities in other hematological

Table 1: Comparison of laboratory and radiological abnormalities amongst younger and older patients

Parameter		Total (n=166)	Younger than 36 years (n=86)	Older than 36 years (n=80)	*P*
Thickened gall bladder wall		67 (40.36%)	40 (46.51%)	27 (33.75%)	0.094
Ascites		49 (29.51%)	31 (36.04%)	18 (22.50%)	0.056
Hepatomegaly		82 (49.39%)	46 (53.49%)	36 (45.00%)	0.027
Splenomegaly		37 (22.28%)	20 (23.25%)	17 (21.25%)	0.756
Pleural effusion	Unilateral	24 (14.45%)	19 (22.09%)	05 (06.25%)	0.014
	Bilateral	24 (14.45%)	12 (13.95%)	12 (15.00%)	
Haemoglobin (g/dL)		11.96±2.46	12.19± 2.51	11.72± 2.41	0.214
Total leucocyte count (x10^9/µl)		4.55± 1.37	4.371± 1.28	4.73± 1.44	0.088
Platelets (x10^9/µl)		97.09± 43.10	89.15± 47.80	93.18± 37.59	0.545

Table 2: Relationship of different hematological parameters wit h clinical and ultrasonographic features

	Hemoglobin			Total Leucocytes Count			Platelets		
Parameter	**Normal (n=55)**	**Low (n=111)**	***p***	**Normal (n=112)**	**Low (n=54)**	***P*-value**	**Normal (n=19)**	**Low (n=147)**	***p***
Duration of illness	7.30± 1.81	7.33± 1.90	0.030	7.29± 1.91	7.38± 1.77	0.784	7.21± 1.58	7.33± 1.90	0.759
Duration of hospital stay	7.13± 1.68	7.08± 1.97	0.868	7.14± 1.92	7.01± 1.79	0.677	5.34± 1.51	7.33± 1.80	<0.001
Thickened gall bladder wall	23	44	0.788	50	17	0.105	0	67	<0.001
Ascites	15	34	0.655	35	14	0.481	0	49	0.001
Hepatomegaly	25	57	0.474	56	26	0.823	8	74	0.499
Splenomegaly	14	23	0.490	26	11	0.680	8	29	0.027
Pleural effusion (unilateral)	8	16	0.904	19	5	0.393	0	24	0.013
Pleural effusion (bilateral)	7	17		15	9		0	24	

cell lines. The relationship of different hematological parameters with clinical and ultrasonographic features is shown in detail in Table 2.

Discussion

A total of 166 individuals were included in our study; all were either Dengue NS-1 antigen positive or antibodies IgM positive against the dengue virus. In our patients, hepatomegaly was the most common ultrasonographic finding, followed by gall bladder thickness, ascites, pleural effusion, and splenomegaly. The ultrasonographic findings were more in the younger age group. The patients with lower platelet counts had longer stay at the hospital. So, ultrasound is a non-invasive modality that helps assess patients with DF. Mosquitoes that bite an infected family member may infect other household members. If someone in your household develops dengue fever, you should be vigilant about mosquito protection measures.[9]

Ibrahim et al. used ultrasound to detect the third spacing of fluid in the leaky phase of dengue. edema of the gall bladder wall was the commonest finding.[10]

Our results are comparable to those reported by Halawar et al. study; the incidence of edema of the gallbladder wall was ranging from 32% to 89%. In 28.91% of our patients, USG revealed pleural effusion, 40.36% gall bladder wall edema, 29.59% ascites, 49.39% hepatomegaly, and 22.28% splenomegaly.[11]

Gayatri et al. conducted a study in India during the dengue epidemic in 2018. The findings of our study were like his study; the only difference was in the most common finding among the included individuals. Our study had hepatomegaly as a common finding, whereas pleural effusion was the,most typical finding in his study.[12]

Malleshappa et al. conducted research to study the role of ultrasound in assessment of patients with dengue fever. According to this study, ultrasound is a good and effective investigation of choice for for diagnosing and grading the severity of illness in patients with DF. The focus was to detect and diagnose leaky phases in a timely to manage patients aggressively to lower the mortality rate. Similar results were found in our study, including hepatomegaly, splenomegaly, gall bladder wall edema, and pleural effusion.[13]

Khurram et al. conducted an observational retrospective study in 2013 on confirmed cases of dengue fever. All cases were serologically confirmed cases with positive dengue NS-1 antigen. Every ultrasound of the chest and abdomen was done in every patient. Our study has similar results, except the rate of pleural effusion was higher in this study.[14]

In 2006, a study was conducted on the outbreak of dengue in India. This study included 169 patients, and an ultrasound was performed on all patients to detect fluid. Our ultrasound findings are also quite like this study.[15]

In 2008, an interesting study was conducted in the United States. It was an experimental study in which 15 individuals were included. After informed consent, an injection of a strain of dengue virus was inoculated in 12, and a placebo was given in 3 individuals. None of the individuals given a placebo showed any findings or any complications, whereas the 7 out of 12 individuals infected with the virus showed complications, including third spacing of fluid confirmed by ultrasound.[16]

In a retrospective study done in Indonesia by Imaniar Noor et al, as per this study, the low platelet counts is a predictor of dengue severity, and the mean platelet count was 91.28± 47.45 x109/µl. the patients with low platelet counts develop dengue hemorrhagic fever. In our study, the mean platelet count was 97.09± 43.10 $x10^9$/µl, and stay of the hospital was longer in patients with low platelet count.[17]

Jayanthi et al. conducted a study in one of the hospitals in India to co-relate effects of thrombocytopenia with rate of complications and hospital stay. The results were like our study as the complication rate and prolonged stay at the hospital was higher in patients with low platelet count.[18]

Malavige et al. studied the role of proinflammatory markers and cytokines on the development of third spacing of fluids; the patients with low platelet count developed more plasma leakage into third space. these findings are like our study as patients with low platelet count showed more sonographic changes in our study group.[19]

Shiyana Ibrahim et al., in their study included patients with fever and thrombocytopenia during an epidemic of dengue in Siri Lanka in 2009.as per his study there was no relationship between thrombocytopenia and hospital stay. These findings are different from our study.[20]

Limitations

Our study was conducted in a single center, and a limited number of patients were included in our study; children were not included in our study, and the number of females was few as compared to males. only indoor patients were included in our study; outdoor patients were excluded. We need more studies at different centers to make protocols for managing dengue epidemics.

Conclusion

Sonographic abnormalities such as edema of the gallbladder wall, hepatomegaly, ascites, pleural effusion, and splenomegaly are found to be the earliest consequences of dengue fever, which can be easily detected by bedside ultrasound. It can be seen that hepatomegaly and unilateral pleural effusion were more common among younger patients. Patients with a lower platelet count had a longer duration of hospital stay, as well as the occurrence of various ultrasonographic abnormalities.

Authors Contribution

AR: Manuscript writing and proof reading
AF: Manuscript writing and proof reading
ARA: Manuscript writing and proof reading
ARA: Manuscript writing and proof reading
WA: Data collection
YA: Data collection

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