

EVALUATION OF ULTRASONOGRAPHY AS AN ADJUNCT FOR DIAGNOSIS OF DENGUE FEVER AMONG CHILDREN: A PROSPECTIVE STUDY.

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Abstract

Introduction :

This study aims to evaluate the role of ultrasonography (USG) for early diagnosis of clinically suspected dengue fever before it becomes serologically positive and the usefulness of USG in predicting the severity of the disease.

Methods:

Prospective observational study conducted at a tertiary care hospital from April 2020 to March 2021, 70 cases of clinically suspected dengue within the age group of 6 months to 15 years presenting with fever for less than 5 days underwent whole abdomen and chest ultrasonography. For seropositive cases, ultrasonography findings and their utility in early diagnosis and prediction of disease severity were analyzed along with their correlation to the clinical and laboratory profiles.

Results :

75.8% had primary dengue and 24.2% had secondary dengue. 94% of cases demonstrated ultrasonography features suggestive of dengue-like hepatomegaly (81%), ascites (63.8%), splenomegaly (56.9%), gall bladder wall thickness (46.6%), Cholecystitis (44.8%) and Pleural effusion (41.4%). Ascites and pleural effusion correlated well with clinical severity ($p < 0.05$). Ascites also had a significant correlation with increased hematocrit ($p = 0.040$) and thrombocytopenia ($p = 0$). A significant correlation was observed between pleural effusion with decreased platelet count ($p = 0.004$) and decreased serum sodium levels ($p = 0.044$). Gall bladder wall thickening > 5 mm correlated well with disease severity. USG showed 94.3% sensitivity, 16.67% specificity, and 81.43% of diagnostic accuracy in the seropositive cases of this study.

Conclusion :

Ultrasonography is useful not only as an adjuvant for early diagnosis of Dengue fever but also as a marker of disease severity

Recommendations

It warrants further community-based studies including pediatric Covid cases.

Keywords: Dengue, Disease severity, Early diagnosis, Seropositive, Ultrasonography, Submitted: 2023-06-01 Accepted: 2023-06-05

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1. Introduction:

Dengue is endemic in more than 100 countries, which are included in the world health organization (WHO) regions of the world.¹ Dengue is deemed second in importance to malaria, the WHO counts Dengue as one of sixteen neglected tropical diseases.^{2,3}

Studies show that the sensitivity rate of NS1(Non-structural protein1) antigen is high in primary dengue (97.41%) than in secondary dengue (68.8%).^{4,5,6,7} With the availability of ultrasonography, diagnosis of dengue can be made as early as third day which could be lifesaving.^{8,9,10,11} Ultrasonography is an adjunct to clinical profile in the diagnosis of dengue fever.^{11,12,13,14,15,16,17}

In pandemic situations like the current Covid-19(Corona virus disease19) crisis, the feasibility of a non-invasive and relatively simple investigation like USG as an adjunct for early detection and an indication of disease severity can be useful for time management and ultimately reduction in mortality due to dengue.

This study aims to evaluate the role of ultrasonography (USG) for early diagnosis of clinically suspected dengue fever before it becomes serologically positive and the usefulness of USG in predicting the severity of the disease.

2. Methods:

This prospective observational study was conducted at a tertiary care hospital Rich Hospitals, Nellore in South India from April 2020 to March 2021.

2.1. Ethical issues:

Approval for the study was obtained from the Institutional Ethics Committee of Rich Hospitals, Nellore, and Andhra Pradesh, India (NO-RICH/RES/2020/048). Written Informed consent was obtained from the parents of the children included in the study.

2.2. Inclusion criteria:

Children between 6 months and 15 years clinically suspected of dengue with a fever of less than 5 days who were, later on, proved serologically positive for dengue fever.

2.3. Exclusion criteria:

Age less than 6 months and more than 15 years, Clinical and Laboratory profile suggestive of dengue but negative for Immunoglobulin G (IgG) and immunoglobulin M (IgM) serology, Children with Dengue managed as an outpatient, those who refused to join to study and duration of fever more than 5 days.

In this study, for the 70 children who had features suggestive of dengue, detailed history of presenting complaints was recorded in a pre-structured proforma. All the children enrolled in this study were subjected to whole abdomen and chest ultrasonography on the day of presentation to the hospital and dengue serology IgM and IgG were done after 5 days of fever. Among these cases, 58 who were found to be seropositive, underwent laboratory investigation after 5 days of fever. Ultrasonography was done using a Toshiba aplio XV ultrasonography machine with a 3.5 MHz curvilinear transducer probe by a qualified radiologist. All children underwent laboratory investigations like complete blood count, serum electrolytes, liver function test, and dengue serological marker along with chest x-ray(CXR). Based on clinical and laboratory features, these children were classified as per WHO classification¹, for these seropositive cases, abdominal ultrasonography findings and their utility in early diagnosis and prediction of disease severity were analyzed along with their correlation to the clinical and laboratory profiles. There were no dropouts in the study population.

2.4. Statistical analysis:

This data was statistically analyzed using SPSS 16.0 and open Epi2.3.1 packages. Various statistical tools/measures like Pearson chi-square test, fisher's exact chi-square test, sensitivity, specificity; positive predictive value, negative

predictive value, and diagnostic accuracy were applied to authenticate the result.

3. Results:

In the present study, children aged above 10yrs were the most common age group (36.2%) while children below 1yr of age were least affected. Out of the 70 children enrolled in this study, 58 were seropositive while 12 were seronegative. These 12 children had nonspecific USG features like mesenteric lymphadenitis, pancreatic enlargement, and liquid within the Morrison's pouch which could not be considered indicative of dengue.

Of the 58 children with seropositive dengue, 75.8 % had primary dengue, 24.2% had secondary dengue, and the distribution of the clinical features in the study sample is as given in Table 1. 55(94%) cases demonstrated ultrasonography feature suggestive of dengue. The ultrasonography findings noted were hepatomegaly (81%), ascites (63.8%), splenomegaly (56.9%) gall bladder wall thickness (46.6%), cholecystitis (44.8%) and pleural effusion (41.4%). The vomiting had a significant correlation with ascites & hepatomegaly. Tachypnea had a significant correlation with splenomegaly. USG findings like ascites ($p < 0.05$) and pleural effusion ($p < 0.05$) correlated well with clinical severity [Table 2]. Clinical & ultrasonography features of ascites had significant correlation. Clinical pleural effusion had a significant correlation with ultrasonography features like ascites, pleural effusion, gall bladder wall edema, cholecystitis, and splenomegaly.

On comparison of USG features with laboratory parameters, ascites had a significant correlation with increased hematocrit ($p = 0.040$) and marked significance with ($p = 0.00$) with thrombocytopenia. A significant correlation was observed between pleural effusion with decreased platelet count ($p = 0.004$) and decreased serum sodium levels ($p = 0.044$). Gall bladder wall thickening had a significant correlation with increased hemoglobin level ($p = 0.013$), increased packed cell volume ($p = 0.021$), and decreased platelet count ($p = 0.005$). Gall bladder wall thickening $> 5\text{mm}$ correlated well with severity [Table 3]

USG showed 94.3% sensitivity, 16.67% specificity and 81.43% of diagnostic accuracy in the seropositive cases of this study. [Table 4]

More than 90% of cases had thrombocytopenia defined as a platelet count less than 1,500,000. Among this 31% had less than 50000, 37.9% had platelet between 50 to 1 lakh and 2 children had a platelet count of 20000. Platelet count of $< 1,00,000$ had a sensitivity of 63.9% and specificity of 75%. Ultrasonography evidence of plasma leakage was most sensitive with 65.52% observed among those having platelet count < 1 lakh. Taking all factors into consideration, platelet count < 1 lakh was the best marker with a diagnostic accuracy of 65.71% followed by ultrasonography with 62.86% [Table 4].

Ultrasonography evidence of plasma leakage viz ascites and pleural effusion was compared with other factors such as Packed Cell Volume, platelet count, and CXR [Table 4]. When all ultrasonography findings were considered together, the sensitivity was 94.83%, specificity 16.67%, and diagnostic accuracy 81.43% [Table 3].

4. Discussion

4.1. USG findings in the study population.

The present study showed the incidence of hepatomegaly (81 %) similar to Balasubramaniam¹⁹ and Rajib et al⁸. However Syed et al found hepatomegaly only in 30% of cases due to low dengue positive cases [$n = 50$]. The present study showed the incidence of ascites (63.8%) similar to studies done by Balasubramaniam¹⁹, Motla¹⁰, Rajib⁸, and VenkataSai⁹ et al. Studies done by Sachar²⁰ et al and Thulkar²² et al had the highest and lowest percentage of patients with ascites respectively. The incidence of splenomegaly (56.9%) in the present study was the highest among comparable studies with other studies consistently showing an incidence of $< 40\%$. Incidence of gall bladder wall thickening in the present study (46.6%) was similar to those undertaken by Wahab¹⁵, Srikiatchon¹², Wu¹⁹, and Thulkar²² et al., whereas Venkatasai⁹ et al found gall bladder wall thickening in 100% of cases. Pleural effusion (41.4%) was found in a similar percentage of patients as

Table 1: Distribution of clinical features of dengue based on WHO classification.

| DENGUE CLASSIFICATION AS PER WHO | CLINICAL FEATURES | FREQUENCY |
|------------------------------------|------------------------|-----------|
| DENGUE (with/without warning sign) | Severe headache | 6 |
| | Pain behind the eyes | 0 |
| | Muscle and joint pains | 7 |
| | Nausea | 0 |
| | Vomiting | 0 |
| | Swollen glands | 0 |
| | Rash | 19 |
| | Severe abdominal pain | 11 |
| | Persistent vomiting | 14 |
| | Rapid breathing | 7 |
| SEVERE DENGUE | Bleeding gums | 3 |
| | Fatigue | 0 |
| | Restlessness | 0 |
| | Blood in vomit. | 7 |

Table 2: Ultrasonography finding based on clinical severity

| Ultrasonography finding | Dengue without warning sign N=12(20.7%) | | Dengue with warning sign N=31(53.4 %) | | Severe dengue N=15(25.9%) | | Total N=58(100%) |
|------------------------------|--|------|--|------|------------------------------|------|---------------------|
| | Number | % | Number | % | Number | % | |
| Ascites | 1 | 8.3 | 22 | 70.9 | 14 | 93.3 | 37 |
| Pleural effusion | 0 | 0 | 13 | 41.9 | 11 | 73.3 | 24 |
| Gall bladder wall thickening | 1 | 8.3 | 15 | 48.4 | 11 | 73.3 | 27 |
| Cholecystitis | 2 | 16.6 | 15 | 48.4 | 9 | 60 | 26 |
| Hepatomegaly | 8 | 66.7 | 27 | 87 | 12 | 80 | 47 |
| Splenomegaly | 5 | 41.6 | 18 | 58 | 10 | 66.6 | 33 |

Table 3: Correlation of USG findings with various laboratory parameters in those with disease severity

| USG parameter | Low platelet | High pcv | High Hb | Low sodium |
|------------------------------|--------------|----------|---------|------------|
| Ascitis | 0.0* | 0.04* | 0.08 | 0.198 |
| Pleural effusion | 0.004* | 0.091 | 0.08 | 0.044* |
| Gall bladder wall thickening | 0.005* | 0.021* | 0.013* | 0.081 |
| Cholecystitis | 0.728 | 0.135 | 0.103 | 0.356 |
| Hepatomegaly | 0.387 | 0.855 | 0.813 | 0.87 |
| Splenomegaly | 0.417 | 0.149 | 0.171 | 0.994 |

* p value more than 0.05 is significant

Table 4: Comparison of sensitivity and specificity of different parameters for diagnostic accuracy of Dengue

| Parameter | Clinical | Pcv>45 | Platelet count < 1 lakh | Ultrasonography (all features as mentioned in Table 1) | Ultrasonography Plasma leakage (ascites, Pleural effusion alone) | Chest x-ray |
|---------------------------|----------|--------|-------------------------|--|--|-------------|
| Sensitivity | 20.69% | 6.89% | 63.9% | 94.83% | 65.52% | 12.07% |
| Specificity | 100% | 100% | 75% | 16.67% | 50% | 100% |
| Positive predictive value | 100% | 100% | | 84.62% | 86.36% | 100% |
| Negative predictive value | 20.69% | 18.18% | | 40% | 23.08% | 19.05% |
| Diagnostic accuracy | 34.29% | 22.86% | 65.71% | 81.43% | 62.86% | 27.14% |

Wahab¹⁵, Motla¹⁰, Wu²¹, and Thulkar²² et al. The percentage of patients with pleural effusion was highest in VenkataSai⁹ et al and lowest in Syed¹⁸ et al. Pericardial effusion, Peri/pararenal fluid collection, and hepatic/splenic subscapular fluid collection were not observed in the present study.^{23,24}

4.2. Correlation of USG features with clinical features and laboratory features.

Hepatomegaly was found in 33 cases clinically but was picked up in 47 cases on ultrasonography while splenomegaly was found in 10 cases clinically but was found in 33 cases on ultrasonography. Similarly, clinical evidence of ascites and pleural effusion was found in 7 and 10 patients respectively while ultrasonography evidence was seen in 37 and 24 patients respectively. Similar findings were observed in Wahab¹⁵ et al.

Similarly, USG picked up more cases of pleural effusion than chest X-ray (24 compared to 10), a trend also observed by Wahab¹⁵ et al and Thulkar²² et al.

4.3. Dengue severity.

Of the 58 children with seropositive dengue, 75.8 % of the cases had primary dengue and 24.2% had secondary dengue, which was similar to those found by Syed et al¹⁸, however, Srikiatchon¹² and Rajib⁸ et al found the majority had secondary dengue [Table 5].

Our study comprised of 25.9% of severe dengue; which was similar to disease distribution in studies by Srikiatchon¹² and VekataSai et al⁹ [Table 5].

Ultrasonography finding like ascites, pleural effusion, and gall bladder wall thickening significantly correlated with abnormal laboratory parameters like low platelets, high packed cell volume, high hemoglobin, and low serum sodium showing their implication in the severity of the disease. Gall bladder wall thickening >5mm correlated well with severity. The present study also found that the incidence of Gallbladder wall thickening, ascites, pleural effusion, hepatomegaly, and splenomegaly increased with the severity of the disease.[Table 2] This is similar to the findings of Wahab¹⁵ et al, and Setiawan¹³ et al. However, peri/Para renal fluid collection, hepatic and splenic subscapular fluid collection which was described in previous studies to be associated with disease severity was not found in the present study. USG evidence of plasma leakage had the highest sensitivity (65.52%) and specificity (50%) compared to clinical evaluation, hematocrit, and chest radiography [Table 4].

Other laboratory parameters were not significant correlation with ultrasonography findings, hence no implication in the severity of the disease [Table 2].

Early identification of the suggestive ultra-

Table 5: Comparison of types & severity of Dengue in this study with other studies

| Study | Primary dengue (%) | Secondary dengue (%) | severe dengue (grade 3 & grade 4) (%) |
|---------------------------------|--------------------|----------------------|---------------------------------------|
| This study | 75.8 | 24.2 | 25.9 |
| Syed et al ¹⁸ | 86 | 14 | 10 |
| Srikiatchon et al ¹² | 13.4 | 86.6 | 25.6 |
| Rajib et al ⁸ | 0 | 100 | 16.7 |
| Iskander et al ²³ | 52 | 48 | - |
| Colbert ²⁴ | - | - | 15 |
| Venkata sai ⁹ | - | - | 26.1 |
| Wahab ¹⁵ | - | - | 17 |

sonography features and management including close observation or monitoring in pediatric intensive care may reduce mortality as suggested by WHO. In the present study, apart from fever (100%), only a few clinical manifestations were observed under dengue with /without warning sign classification based on the world health organization in the early stage of the disease [Table 1]. However, ultrasonography identified more cases of dengue with/without warning signs as shown in [Table 2]. Almost 15(25.9%) cases of severe dengue, 31(53.4%) cases of dengue with warning signs, and 12(20.7%) cases of dengue without warning signs were predominantly identified with ultrasonography in less than five days. In this study only one case of shock and seizure manifestation was reported, based on the ultrasonography report, these children were closely monitored and all children recovered without any morbidity and mortality.

5. Limitations of the study:

It is a single center-based study where the study population may not be representative of the entire community.

6. Recommendations:

It warrants further community-based studies including pediatric Covid cases.

7. Conclusions:

It can be concluded that ultrasonography is an important adjuvant to clinical profile in the diagnosis of dengue. Especially in underdeveloped and developing areas which are endemic with less availability of serological studies and also in Pandemic situations as in the present ongoing COVID-19 and Multisystem Inflammatory Syndrome in Children (MIS-C), where dengue fever is a differential diagnosis, where noninvasive investigation like ultrasonography can help to clinch the diagnosis. Therefore, it can be concluded that not only ultrasonography is useful as an adjuvant to early diagnosis of Dengue fever where the serologic diagnostic facility is not readily available but also as a marker of disease severity. Early diagnosis of dengue features by ultrasonography helps in prioritizing the modality of management thus decreasing the mortality rates.

8. Conflict of Interest:

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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