Ultrasound Features of Dengue and its Correlation with Platelet Count

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Abstract: *Aim: Correlation of sonographic features of polyserositis with platelet counts in dengue fever. Materials & Methods: Three hundred patients with positive dengue serology [160 (54%) males and 140 (46%) females], in the age group of 3-80 years, were evaluated by trans abdominal sonography during an epidemic from March 2017 to October 2017 in a tertiary care hospital. The findings were correlated with platelet counts. Results: The common features on ultrasonography were hepatomegaly, GB wall edema, ascites, splenomegaly and pleural effusion. Hepatomegaly was observed in 72% of the patients (n=216), GB wall edema in 65% (n=195), splenomegaly in 44% (n=132), ascites in 50% (n=150), unilateral pleural effusion in 52% (n=156) and bilateral pleural effusion in 27% (n=81). Conclusion: In a febrile patient with thrombocytopenia and positive dengue serology, ultrasonography of abdomen is a useful tool to evaluate severity of illness. Ultrasound findings of GB wall edema, ascites and pleural effusion are directly proportional to the extent of thrombocytopenia. In an epidemic scenario USG features may help in roughly estimating the platelet count even before serology and platelet results are available. Thus, it helps in treatment planning without waiting for the laboratory results.*

Keywords: Dengue, poly-serositis, ultrasound, GB wall edema

1. Introduction

Dengue Fever is the most common acute arboviral infection in the world, caused by a flavivirus called Dengue virus [1]. It is transmitted by female Aedes egypti mosquito. Its incidence has increased enormously in the recent past and as an important tropical mosquito-transmitted infectious disease, it is surpassed only by malaria [2]. It is endemic in more than 100 countries of the world and threatens the health of 40% of the world's population [3]. It is more common during rainy season due to breeding of mosquitoes facilitated by water stagnation.

The disease occurs in two forms namely the classic dengue which is a milder form of the illness and the severe Dengue Hemorrhagic Fever (DHF). Thrombocytopenia and hemoconcentration are seen in both the forms of the disease. The diagnosis of dengue fever is based on clinical suspicion in endemic areas along with positive serology. Anti dengue antibody appears only after 7 days of the onset of disease, thus delaying the diagnosis [4].

Ultrasonography (USG) is an economical, rapid and widely available non- invasive imaging modality in the diagnosis of dengue fever.Several studies have proven that ultrasonography of the chest and abdomen can be an important adjunct to clinical profile in the early diagnosis of dengue fever[2]. Milder form of the disease shows hepatosplenomegaly and mild gall bladder wall thickening. Severe form of the disease is characterized by fluid collections in the perirenal and para renal spaces, hepatic and splenic subcapsular fluid collections, pericardial effusion, moderate pleural effusion, moderate ascites, significant gallbladder wall thickening, hepatic intraparenchymal haemorrhages and pancreatic enlargement [5,6].

The disease severity is directly related to thrombocyte count and the findings are severe with falling platelet counts [6]. This study has the objectives of sonographically evaluating the abdominal manifestations of dengue fever and correlating the sonographic findings of dengue fever with platelet counts in patients of all age groups. It provides a rough roadmap for treatment planning and prognostication of dengue fever patients.

2. Literature Survey

Dengue is now endemic in more than 100 countries and threatens the health of more than 2500 million i.e. 40% of the world's population. It is estimated that 10 million classic dengue infections occur each year with 500,000 cases of Dengue Hemorrhagic Fever. Its mortality ranges from 1-5% of treated patients to a maximum of 50% for untreated or poorly treated patients resulting in at least 12,000 deaths annually mainly among children [3].

The global prevalence of dengue has dramatically increased in recent decades. The disease is now endemic in more than 100 countries in Africa, Americas, the eastern Mediterranean, South East Asia and western pacific. South East Asia and western pacific are most seriously affected. At least 2.5% cases die, although case fatality could be twice as high. Without proper treatment DHF case fatality can exceed 20% [18].

It is caused by the dengue virus, a flavivirus transmitted by Aedes aegypti mosquito. There are four distinct antigenic types of dengue viruses. Each virus elicits specific lifetime immunity against the same serotype, as well as short term cross immunity against the other three serotypes which may last for several months. All four serotypes can cause severe and fatal disease [19].

The onset of the disease is recognized by the sudden appearance of high fever, retro-orbital pain, myalgia, bone & joint pains, thrombocytopenia and haemorrhagic manifestations. The disease occurs in two forms namely the classic dengue which is a milder form of the illness and the severe Dengue Hemorrhagic Fever (DHF). Thrombocytopenia and hemoconcentration are seen in both the forms of the disease [8].

Common laboratory findings in dengue are neutropenia, haemoconcentration, thrombocytopenia and prolonged bleeding time. Serology is the mainstay in the diagnosis of dengue fever. [8]. Anti dengue antibody appears only after 7 days of the onset of disease, thus delaying the diagnosis [4]. The disease severity is directly related to thrombocyte count and the findings are severe with falling platelet counts [6].

Ultrasonography (USG) is an economical, rapid and widely available non- invasive imaging modality in the diagnosis of dengue fever. Several studies have proven that ultrasonography of the chest and abdomen can be an important adjunct to clinical profile in the early diagnosis of dengue fever [2].

Milder form of the disease shows hepatosplenomegaly and mild gall bladder wall thickening. Severe form of the disease is characterized by fluid collections in the perirenal and para renal spaces, hepatic and splenic subcapsular fluid collections, pericardial effusion, moderate pleural effusion, moderate ascites, significant gallbladder wall thickening, hepatic intraparenchymal haemorrhages and pancreatic enlargement [5,6].

3. Materials & methods

This prospective correlative study was performed in a tertiary care hospital on 300 patients of suspected dengue fever during the epidemic from March 2017 to October 2017. All the patients with fever, myalgia and positive serology (NS1 Ag/ IgM/ IgG) were included in the study. Patients of all the age groups and both the sexes consenting for the study were included. Patients with negative serology were excluded.

The patients were subjected to ultrasonography of the abdomen in supine position on Philips HD 11 XE ultrasound scanner using 3-5MHz convex transducer. The sonographic assessment included evaluation of hepatospleomegaly, gall bladder wall edema, ascites, pleural effusion and any other fluid collection in the abdomen. Standard sonographic techniques and age based criteria were used for the assessment of organomegaly & fluid collections.

The gall bladder wall thickness was measured by placing the calipers between the inner and outer layers of the anterior wall of the gall bladder. A wall thickness of >5mm was considered as thickened irrespective of the prandial status. The patients with gall stones were excluded in the statistical analysis even though they had positive serology and gall bladder wall edema to avoid bias with calculus cholecystitis.

Dengue serology and sonographic findings were correlated with platelet counts. Results were tabulated and analysed statistically using mean, median, standard deviation, Mann Whitney test & Kruskal Wallis test. All the statistical measures were derived using SPSS 21 software.

4. Results

Out of the three hundred patients included in the study, 160 (54%) were males and 140(46%) were females. Serologically, 60 patients (20%) were positive for only NS1 antigen; 60 patients (20%) were IgG & IgM positive; 20 patients (6.7%) were NS1 & IgG positive; 20 (6.7%) were NS1 & IgM positive; 10 (3%) were only IgM positive; 110 patients (36%) were only IgG positive. Twenty patients (6.7%) were positive for all the three serological tests.

The age group of the patients included neonates to octogenarians. However, the disease was common among children and young adults. Patients above 50 years were rare in our study (n =30; 10%). The highest number of cases occurred between 10-35years (n=210; 70%).

The common features on ultrasonography were hepatomegaly, GB wall edema, ascites, splenomegaly and right pleural effusion. Hepatomegaly was observed in 72% of the patients (n=216), GB wall edema in 65% (n=195), splenomegaly in 44% (n=132), ascites in 50% (n=150), unilateral pleural effusion in 52% (n=156) and bilateral pleural effusion in 27% (n=81).

There was an association between the sonographic findings and the platelet count. All the patients with platelet count below 60,000 had hepatomegaly. GB wall edema was invariably present when the counts were below 40,000. Ascites and pleural effusion were common with platelet count less than 30,000. The severity of GB wall edema was more with decreasing platelet count. With severe platelet count reduction (<10,000), GB wall edema was upto 10mm. The presence of perinephric fluid collection also correlated with platelet count. Lower the platelet count (below 40,000), the more was the perinephric fluid collection. There were no sonographic findings related to polyserositis when the platelet counts were above 1 lakh. There was no significant correlation between splenomegaly and platelet counts. But splenomegaly was present in many cases along with hepatomegaly.

Fig.1 & 2: Trans abdominal sonography image demonstrating the GB wall edema.
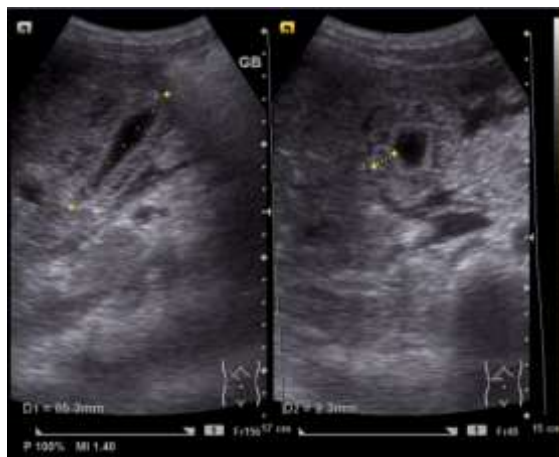

Figure 1

Figure 2

Cases with moderate ascites had a median platelet count of 30000 with the lowest count of 27000 and the highest 60000/cumm. Cases with bilateral pleural effusion had a median platelet count of 27000 with lowest count of 18000 and highest 60000/cumm. Cases with unilateral pleural effusion had median platelet count of 50000 with lowest count of 33000 and highest 60000/cumm. Cases with GB wall edema, pleural effusion and ascites had a lowest platelet count of 18000 and highest 60000 with a median platelet count of 27000/cumm. Cases with splenomegaly had no significant correlation with platelet counts.

Table 1: Correlation of median platelet count and sonographic findings

S.No	Median Platelet Count	Sonographic Finding
1.	60,000 and below	Hepatomegaly
2.	40,000 and below	GB wall edema
3.	30,000 and below	Ascites and right pleural effusion
4.	27,000 and below	Bilateral pleural effusion

5. Discussion

Dengue fever is an acute flavi viral infection which occurs either as the milder dengue fever or the severe dengue hemorrhagic fever. Frequency of dengue is increasing due to uncontrolled population growth, improper urbanization, inappropriate water management, global spread of dengue strains via travel and erosion of vector control programs [15]. This study was conducted in a tertiary care hospital during one such epidemic.

Dengue viruses are transmitted to humans through the bite of infected female Aedes mosquito. The incubation period is 3–14 days. The onset of the disease is recognized by the sudden appearance of high fever, retro-orbital pain, myalgia, bone & joint pains, thrombocytopenia and haemorrhagic manifestations [8]. In our study also, all the patients had fever, myalgia and variable degrees of thrombocytopenia. Common laboratory findings in dengue are neutropenia, haemoconcentration, thrombocytopenia and prolonged bleeding time [8]. Serology is the mainstay in the diagnosis of dengue fever. All the patients with positive serology were included in our study.

The major pathophysiological feature of DHF is an increased vascular permeability, giving rise to loss of plasma and albumin from the vascular compartment. Early diagnosis and treatment of DHF can definitely ameliorate the complications of the disease such as haemorrhage, hypovolaemia and shock [13]. The severe forms of dengue fever occur when there is infection by more than one serotype of the virus. The first infection sensitizes the immune response and the superadded infection induces severe immune response [15].

A diagnostic test that can quickly detect endothelial damage and facilitate immediate treatment is not currently available and the serological test needs paired serum samples with an interval of at least 7 days [13]. Ultrasound can be used to detect small amounts of transudate in serous cavities in patients suspected of having DHF in endemic regions. Although not specific, the sonographic findings in dengue are obtained more rapidly than the results of serologic tests. The early sonographic findings of DF have rarely been reported in the literature [12].

The aim of the this study was to evaluate the ultrasound findings in Dengue fever, to find whether ultrasound of the abdomen is an important adjunct to laboratory profile (platelet count and serology tests) in diagnosing Dengue fever and further if ultrasound is useful in predicting the severity of the disease.

GB wall edema:
Even though a non specific finding, the presence of GB wall edema indicates polyserositis in patients with suspected dengue fever. Khalid Rehman et al [6] have shown that GB wall edema was the most consistent finding (63%) on abdominal sonography in patients with dengue fever. Vedaraju et al have observed GB wall edema in 83% of cases of dengue fever [9]. Thickened gall bladder wall was the most common feature in dengue patients in the studies conducted by Keng-Liang Wu et al {[1], M VenkataSai Et al [11] Melani W. Setiawan [16] and Mia MW et al [17]. In the our study also, 65% of the patients had GB wall edema with a median platelet count of 40000/ mm^3.

GB wall edema is also seen in hepatitis, ascites, cholecystitis, hypoalbuminemia, chronic liver disease, renal failure etc [8]. Its presence in the background of positive dengue serology indicates severe dengue fever. However to avoid bias due to calculous cholecystitis, the cases with cholelithiasis were excluded in the statistical analysis of our study. The statistical significance of GB wall edema and low platelet count was very high in our study (P<0.0001).

Hepatomegaly:
Hepatomegaly is also a non specific finding, seen in hepatitis, systemic infection, cardiac failure etc. Santosh et al [10] found that sonographic findings of DF were thickened gallbladder wall, ascites, hepatosplenomegaly, and pleural effusion. In our study also hepatosplenomegaly, GB wall edema, ascites and pleural effusion were observed. Infact, hepatomegaly and GB wall edema were the most common sonographic findings in our study. Hepatomegaly was observed in 72% of the patients in our study.

Pleural effusion and ascites (Plasma leakage features):
In the study of Melani W. Setiawan [16], pleural effusion

was bilateral in 43%, right-sided in 20% but never only on the left side. In our study, right sided pleural effusion was present in 52% and bilateral effusion was observed in 27% of the patients. Only one case of isolated left sided pleural effusion was observed in our study.

Venkata Sai et al [11] have observed increase in the severity of polyserositis findings on serial ultrasound studies done on 3rd and 7th day of onset of fever. However, in our study, serial ultrasound studies were not performed routinely. Repeat ultrasound examination was performed only in those patients showing clinical deterioration. Chandrajeet et al [14] and Muhammad Khurram et al [13] have observed that ultrasound is a useful tool in the diagnosis of plasma leak features. They documented pleural effusion and ascites as the evidence of plasma leak in their study. In our study also, pleural effusion and ascites were observed. Ascites was seen in 50% of the patients. The correlation between low platelet count and ascites was statistically significant in our study (P<0.03).

Nataraj et al [7] have reported multiple atypical manifestations like encephalitis, polyneuropathy, myocarditis etc in a few patients with dengue fever. In our study only one case of dengue encephalitis was observed. The other rare manifestations were not observed in our study. The cause of the occurrence of these atypical manifestations is not clear and probably related to immunological response.

The findings of polyserositis occur only when the platelet counts fall significantly. In our study, no findings of polyserositis were seen in patients with platelet count above 1 lakh. This is in consistency with studies of Santhosh et al [10] and Kanaga Durga et al [12].

Thus, our study correlates the extent of polyserositis on sonography with thrombocytopenia on laboratory studies. Considering the ultrasound findings in a suspected case of dengue fever, the rough estimate of the platelet count can be made, without having to wait for the serology & laboratory results. The mainstay of treatment in dengue fever is maintenance of hydration. This study provides correlation of ultrasonographic findings with platelet counts and thus helps in quick treatment planning.

6. Conclusion

In a febrile patient with thrombocytopenia and positive dengue serology, ultrasonography of the abdomen acts as a very useful tool to evaluate the severity of the illness. Ultrasound findings of GB wall edema, ascites and pleural effusion are directly proportional to the extent of thrombocytopenia. In an epidemic scenario, the findings in our study may help in roughly estimating the platelet count even before serology and platelet results are available. Thus, it helps in treatment planning without waiting for the laboratory results. This may save a lot of crucial time for handling the epidemic efficiently.

7. Future Scope

Ultrasonography can be used as an adjunct to clinical and laboratory investigations in dengue fever. As the serological diagnosis takes about 7 days, sonography can help in quick diagnosis of plasma leak manifestations of dengue fever early in the course of the disease.

Studies on large number of people may be conducted during the epidemics and strain based virulence can be evaluated by correlation of the strain of virus and sonographic findings.

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