

DISCUSSION

It is challenging to differentiate early stage of GD from GTT in thyrotoxic pregnant patients in early pregnancy on the basis of nonspecific clinical features because of the absence of specific signs, such as ophthalmopathy, skin and nail changes. Inappropriately managed Graves' disease during pregnancy can cause serious complications in both the mother and the fetus, such as low birth weight babies, preterm births and congenital malformations (2,5). Therefore, early diagnosis is essential for appropriate management plan.

Despite high cost and limited availability, RAIU is a gold standard and radioisotope scan of thyroid gland a widely used diagnostic tool for diagnosis of GD. But, the detrimental effect of ionizing radiation on pregnancy restricts its application. TRAb level also can help in aetiological differentiation of thyrotoxicosis in difficult situations (4, 8), while TSH receptor- stimulating immunoglobulin bioassays are also costly and time-consuming. CFDS by ultrasonography, a cost-effective, portable, safe, and noninvasive method, is now widely used to measure tissue vascularization and blood flow velocity and helps in assessing thyroid gland functional status indirectly (9). Compared with thyroid CFDS judgment, STA-PSV detection has been reported as more objective and accurate (10). A diagnostic meta-analysis of 11 studies with 1052 cases of Asian population, showed the pooled sensitivity and pooled specificity of STA-PSV by ultrasonography were 0.86 (95% CI, 0.80–0.90) and 0.93 (95% CI, 0.86–0.97) in distinguishing GD from destructive thyroiditis, respectively, with the AUC of 0.94 (95% CI, 0.92–0.96). In question of discriminating GTT from GD during pregnancy by means of arterial flow velocity, our study shows, the mean right and left STA-PSV in patients with GTT was significantly lower than

that in pregnant patients with GD and slightly higher than that in healthy euthyroid subjects.

A significant and positive correlation between the serum TRAb level and STA-PSV has been reported in patients with relapsed history of GD (11). Another study also showed association of increased STA-PSV and high levels of TRAb in the relapsing form of GD and suggested that thyroid hypervascularization was most likely related to the activity of the underlying autoimmune processes (12). Correlation between colour Duplex and Tc-99m thyroid scan in identifying the cause of toxic goiter has also been reported in another study (13). In the current study, we also found a positive correlation between STA blood flow velocities and TPOAb levels which has not done before.

There were some limitations of the study. Firstly, the sample size was very small. Secondly, further subgroup (as nonpregnant patients with GD or pregnant euthyroid subjects) analysis could not be performed due to a small number of included diagnostic studies and patients. Again, all pregnant patients with thyrotoxicosis were diagnosed with GTT and GD based mainly on the TPOAb level results, although TRAb is the more appropriate and specific test for GD. Again, fifteen healthy euthyroid subjects had PSV of STA lower than the mentioned normal reference range in other studies (13). However, this preliminary study suggests that quantitative data of thyroid blood flow velocity by ultrasonographic CFDS might be a useful tool to discriminate GD from GTT in thyrotoxic pregnant patient.

CONCLUSION

STA-PSV by ultrasonography can be an acceptable alternative diagnostic method for the differentiation of GD from GTT during pregnancy even in rural areas where other modality are not available. More studies are needed for further

evaluation of the diagnostic accuracy of STA-PSV for the differential diagnosis of thyrotoxicosis during pregnancy.

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Ultrasound Features In Dengue Fever: A Preliminary Experience At INMAS, Faridpur

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Dengue fever is a pattern of febrile illness commonly occurring in tropical regions of the world, including Bangladesh. It is caused by a single stranded RNA virus with four serotypes, and is transmitted via *Aedes aegypti* mosquito. In recent years, there has been a marked increase in the number of reported dengue cases in Bangladesh. This study is aimed at observing the common sonographic features present in dengue fever. In this cross sectional study, a total of 63 patients were included, all of whom were referred to INMAS, Faridpur between August & September 2019, after being clinically and serologically diagnosed as cases of dengue fever. Sonographic examinations of abdomen and chest were done. Concurrent values of complete blood count were also taken into account. The incidences of various findings were calculated and expressed in percentile value. Associations between the variables were also analyzed. Majority of the patients were male (54%) and within the age range 21-40 years (49.2%). The most common finding was thick edematous gallbladder (GB) wall (49.2%), followed by small to moderate ascites (44.4%), and right sided pleural effusion (31.7%), hepatomegaly (27%), splenomegaly (19%), bilateral pleural effusion (12.6%), pericardial effusion (1.6%) and bilateral enlarged kidneys (1.6%). There were no cases with isolated left sided pleural effusion or perirenal collection. The most commonly coexisting features were thick edematous GB wall with pleural effusion (bilateral or right sided) which was found in 33.3% patients. 19% of the patients had sonographically normal abdomen and chest. The presence of any one or a combination of the findings was more common in patients with hematocrit level above 40% and platelet count below 70000.

Presence of thickened GB wall with or without pleural effusion & ascites in a febrile patient may indicate dengue fever and early plasma leakage. Therefore, during an outbreak, it should raise the suspicion of dengue fever and warrant further investigations for early detection and management of complications.

Key words: Dengue fever, Ultrasonography,

Dengue fever is a pattern of febrile illness commonly occurring in the tropical regions of the world, including Bangladesh. Worldwide, clinically apparent dengue fever is estimated to affect 96 million people every year, 500,000 of them having severe form of the disease (1). It is caused by a single stranded RNA virus belonging to flaviviridae family. The virus has four serotypes (DENV-1, DENV-2, DENV-3 and DENV-4), and is primarily transmitted via *Aedes aegypti* mosquito. Infection with one serotype provides prolonged immunity against that

serotype, but increases the risk of developing complications in subsequent infection by another serotype. (1,2)

Dengue fever occurs in varying severities, including classical dengue fever, dengue hemorrhagic fever (characterized by hemorrhagic manifestations i.e. petechial spots, epistaxis, GI tract bleeding, hematuria, menorrhagia etc), and dengue shock syndrome (caused by extensive plasma leakage and hemorrhage leading to hypovolemic shock). Commonly dengue fever presents with high grade fever, anorexia, nausea, vomiting, retro-orbital pain, headache and in most cases, severe myalgia and joint pain. Diagnosis of dengue hemorrhagic fever relies on a positive tourniquet test, and when associated with features of shock, it is regarded as a case of dengue shock

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syndrome. The diagnosis is made on both clinical and serological grounds. Serological tests include detection of NS1 antigen in serum within the first 3-5 days of illness, and detection of immunoglobulin against the antigen from 5th day onwards (2).

In recent years, there has been a marked rise in the number of reported dengue cases in Bangladesh, as well as in other countries of south-east Asia including Philippines, Malaysia and Thailand. During this time increased number of patients was being admitted into hospitals all over the country with varying severities of dengue fever. This study was conducted with an aim to observe the commonly occurring sonographic features in dengue fever, and to determine whether detecting a pattern of features alongside analysis of laboratory values may have any role in predicting the severity of the disease.

PATIENTS AND METHODS

The study was conducted at Institute of Nuclear Medicine and Allied Sciences, Faridpur. It was a

cross sectional type of study conducted between August and September 2019. A total of 63 patients were included in the study. The patients were all clinically and serologically diagnosed as having dengue fever, and were referred to the institute for ultrasound examination. Some of the patients had petechial spots but none had evidence of significant hemorrhage, and all patients were hemodynamically stable.

Sonographic examinations were done between 2nd to 12th day of illness, with a mean of 6.7th day. Machines used were Mindray DC 7 & Phillips affinity 70. 3.5-5 MHz and 7-12 MHz probes were used. Patients were prepared by fasting for at least 6 hours before upper abdominal examination. Abdomen and chest were examined in supine, lateral and prone positions. Per-abdominal and intercostal approaches were used. Presence of abnormalities in abdominal organs, and collection in pleural, peritoneal and pericardial spaces were noted. Concurrent values of complete blood count were also taken into

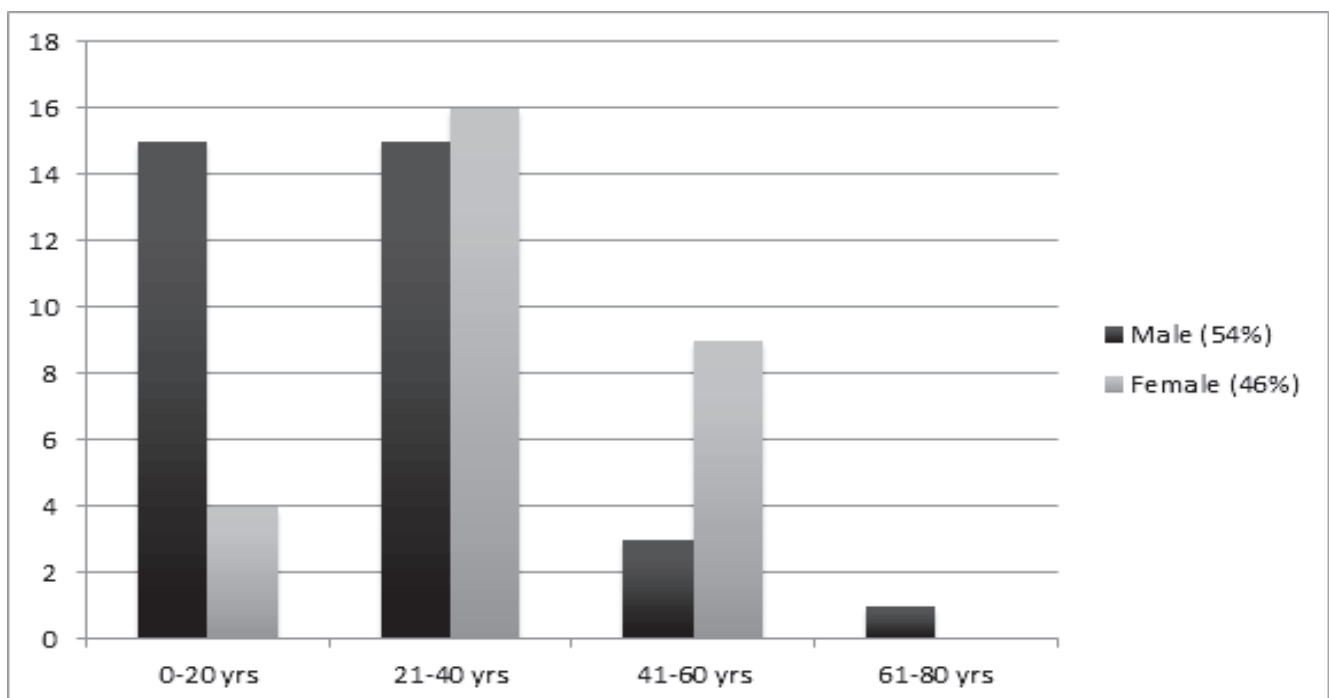


Figure 1 : Age and sex distribution of study population

account. Incidence and association of various findings were analyzed.

RESULTS

Out of the 63 patients in this study, 34 (54%) were male and 29 (46%) were female. Age ranged between 2 to 65 years; including 19 (30.2%) patients between 0-20 years, 31 (49.2%) patients between 21-40 years, 12 (19%) patients between 41-60 years and 1 (1.6%) patient in the 61-80 years range. Most of the patients were within the age range of 21-40 years and mean age was 29.8 years.

Presence of thick edematous gall bladder wall was the commonest finding, which was present in 31 patients (49.2%), followed by pleural effusion

Table 1: Ultrasonography findings of study population

Ultrasonography findings		No. of patients	%
1.	Thick walled edematous gallbladder	31	49.2%
2.	Ascites	28	44.4%
	Mild	24	38.1%
	Moderate	4	6.3%
3.	Pleural effusion	28	44.4%
	Bilateral	8	12.6%
	Right	20	31.7%
	Left	0	0
4.	Hepatomegaly	17	27%
5.	Splenomegaly	12	19%
6.	Pericardial effusion	1	1.6%
7.	Enlarged kidneys	1	1.6%
8.	Normal ultrasonography	12	19%

and ascites, each of which were found in 28 patients and had 44.4% incidence. Among the patients with pleural effusion, 20 patients had isolated right sided pleural effusion (31.7%) and 8

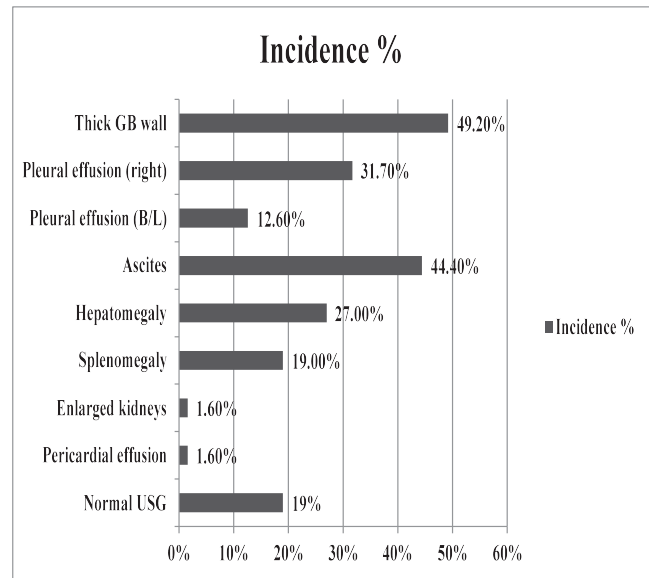


Figure 2 : Incidence of sonographic findings in patients with dengue fever

had bilateral pleural effusion (12.6%). Isolated left sided pleural effusion was not found in any of the patients. Ascites ranged from mild to moderate, with 24 patients having mild (38.1%) and 4 having moderate ascites (6.3%). 17 patients had mild hepatomegaly (27%), and mild splenomegaly was present in 12 patients (19%). Pericardial effusion and bilateral enlarged kidneys were present in one patient each, making the incidence 1.6%, and these were the least commonly found features in our study. 12 (19%) patients had sonographically normal abdomen and chest.

Thick edematous gall bladder wall was also the most common finding in all individual age groups except in the 0-20 years age range, where ascites had the highest incidence (52.6%). The most commonly co-existing features were thickened gall bladder wall with pleural effusion; these two findings co-existed in 21 (33.3%) patients. Thickened gall bladder wall with ascites was found in 17 (27%) patients.

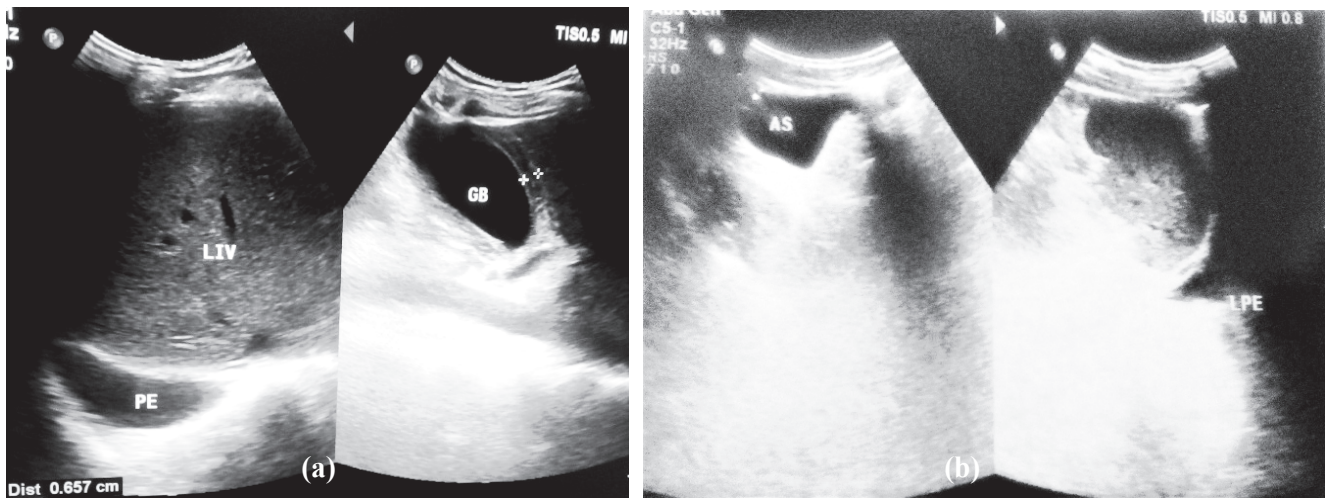


Figure 3: Presence of (a) thick gallbladder wall (6.5 mm), (b) bilateral pleural effusion and ascites in a patient with dengue fever.

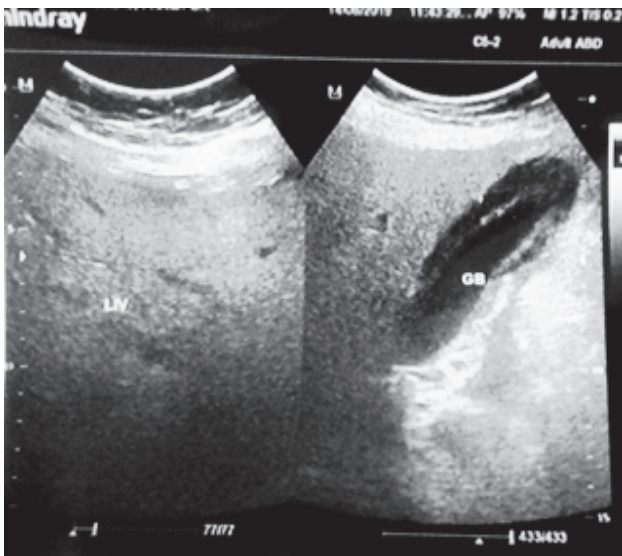


Figure 4: Hepatomegaly and thickened edematous gallbladder wall in a patient.



Figure 5: Presence of thick walled gallbladder and splenomegaly

Abnormal findings were more common in patients undergoing examination within the first 5 days of illness; abnormalities were noted in 16 patients (88.9%) out of 18, with 2 patients having normal findings. Most patients were examined between 6th to 9th day of illness (36 patients), of which 28 (77.8%) had abnormalities.

Table 2: Association between day of illness and ultrasonography findings

Day	Abnormal ultrasonography	Normal ultrasonography
<6 (18)	16 (88.9%)	2 (11.1%)
6-9 (36)	28 (77.8%)	8 (22.2%)
>9 (9)	7 (77.8%)	2 (22.2%)

Majority of the patients presented with thrombocytopenia, with 10 (15.9%) patients having platelets within normal range. Out of the 38 patients with platelets count of $70,000/\text{cm}^3$ or less, 28 had any or a combination of abnormal findings (positive predictive value 73.7%). 25 patients had platelets above $70,000/\text{cm}^3$, and 16 (64%) of them had positive findings. Nearly half of the study population (49.2%) had hematocrit value at or above 40%, of whom 71% presented with positive findings, as opposed to 59.4% of the patients with hematocrit less than 40%. Abnormal findings were more commonly found in patients having hematocrit $\geq 40\%$ and platelet count $\leq 70000/\text{cm}^3$.

DISCUSSION

Dengue fever is an emerging disease in the modern world, estimated to affect 390 million people in varying severities annually. Although Asia shoulders about 70% of the total burden, approximately half of the world population is thought to be at risk. In the past two decades, the incidence has increased over 8 fold, causing the largest global outbreak in 2019 (1). Bangladesh is one of the 100+ countries where dengue fever is endemic. In Bangladesh, the first epidemic occurred in 2000, with 5551 people affected by dengue and 93 reported deaths (1, 2). The outbreak of 2019 in Bangladesh started at around April 2019, and by August 2019, a total of 38,844 people were reportedly affected by dengue (3). Although the majority of cases were reported in the capital, the number of patients outside Dhaka was also significantly high, reaching 12,196 by August, 2019 (3).

Dengue fever progresses from febrile to critical phase in approximately 3 to 7 days (2, 4). Dengue virus has four serotypes, and being affected by one serotype does not give prolonged immunity against other serotypes. In fact, secondary infection by another serotype of dengue virus is thought to be

an important risk factor for developing severe disease. Infection by another serotype causes increased uptake of virus by cells and increased T-Cell activation, causing cytokine release. These cytokines increase the capillary permeability, resulting in plasma leakage and disseminated intravascular coagulation. This along with vascular endothelial damage, platelet dysfunction and thrombocytopenia lead to hemorrhage (2, 4, 5). In addition, it has also been suggested that the antibody against NS1 antigen also shows cross-reactivity against platelets and endothelial cells, which contributes to the damage (4). Severe thrombocytopenia usually precedes the onset of plasma leakage, and as capillary leakage continues, the hematocrit level rises 20% or more from the baseline value (2). Continuing extravasation of fluid often results in pleural effusion and ascites, and may be extensive enough to cause hypovolemic shock. It is therefore crucial to identify the patients at risk of developing these complications, as proper intervention at this stage can reduce the fatality of severe dengue to less than 1% (1).

In our study, the majority of the study population was male, and within 21-40 years age range. Most of the patients were examined after the onset of critical phase (within 6th to 9th day), but the abnormal findings were mostly noted in patients examined within the first 5 days. None of the patients had any clinical evidence of circulatory compromise.

The most common finding in this study was presence of thickened and edematous gall bladder wall. It was also the commonest finding in similar studies conducted by Vedaraju et al, Basawaraj et al & Manam et al (6-8). We found the incidence of abnormal findings to be higher in the 21-40 years age range, while Basawaraj et al found the incidence of abnormality to be more in lower age

groups below 20 years. (7). In our study, thickened GB wall was the commonest finding in all the age groups over 20 years, but in the 0-20 years age group ascites was found to be the most common. This did not concur with the findings of Manam et al, who found pleural effusion and ascites to be more common in patients above 49 years age (8).

The second most common abnormalities that we observed were pleural effusion and ascites, which had equal incidence (44.4%) in our study, though thickened GB wall was more commonly found in association with pleural effusion than with ascites. Several other studies including those done by Vedaraju et al, Thulkar et al and Pramuljo et al described a higher incidence of pleural effusion compared to ascites (6, 9, 10). In fact, pleural effusion was the commonest finding in the study conducted by Thulkar et al which included patients with grade III dengue fever only. However, a study conducted by Motla et al found ascites to have the highest incidence overall (11). These agree with the observation made by Venkata Sai et al that thickened GB wall, pleural effusion and ascites strongly indicate dengue fever during an epidemic (12).

The least common findings in our study were pericardial effusion and bilateral mildly enlarged kidneys which were found in one patient each and in both cases were present in conjunction with pleural effusion, ascites and thickened GB wall in the same patient. However perirenal collection was not seen in any of the patients. This was in contrast to studies done by Basawaraj et al and Setiawan et al who found perirenal collection in dengue patients. Setiawan et al also found presence of pancreatic gland enlargement in 44% of the patients, which was not observed in our study (13).

Several studies done previously had found presence of isolated left sided pleural effusion (6-8), while several others had not encountered this finding (9-11, 13). In the current study, none of the

patients had isolated left sided pleural effusion.

We found the abnormal ultrasound features more commonly in patients with higher hematocrit values (at or above 40%), though evolution of these features with gradually rising or decreasing hematocrit value was not observed. The abnormalities we found were more commonly present in patients having platelet count below 70,000/cm³, and this reflected the observation from a few other studies (6, 8).

CONCLUSION

Effective and timely management of dengue fever requires prompt diagnosis as well as identification of plasma leakage as early as possible. Ultrasound can be a useful non-invasive tool in detecting early signs of complication which may not be apparent clinically. Presence of thickened gall bladder wall with or without pleural effusion & ascites in a febrile patient may indicate dengue fever and early plasma leakage. Therefore, during an outbreak, it should raise the suspicion of dengue fever and warrant further investigations to determine the risk and to take necessary interventions for preventing fatality.

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