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Correlation of radiological findings & hematological findings in assessing severity of dengue fever in pediatric patients

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ABSTRACT *This study was conducted to find out the correlation of radiological findings and haematological findings in assessing severity of Dengue. The study was conducted at Dr D Y Patil medical college Pimpri Pune. 100 serologically diagnosed Dengue fever patients underwent ultrasonography and haematological tests and their findings were correlated. Results as follows Sonographic features of thickened GB wall, pleural effusion (bilateral or right side), ascites, hepatomegaly and splenomegaly should strongly favour the diagnosis of dengue fever in patients presenting with fever and associated symptoms, particularly during an epidemic. The degree of thrombocytopenia showed a significant direct relationship to abnormal ultrasound features (in various combinations) in our study Ultrasound imaging features also showed a relationship to the age of the patient, most common age group affected in our study was age more than 5 years.*

KEYWORDS : Ultrasonography, Dengue Fever, thrombocytopenia, raised hematocrit

INTRODUCTION

Dengue is a mosquito-borne infection that in recent years has become a major international public health problem [1]. Dengue fever (DF) has been known for more than a century in the tropical areas of South East Asia and the Western Pacific regions [2]. Clinically dengue manifests with acute onset of fever, severe headache, retro-ocular pain and pain involving the muscles and joints. Haemorrhagic diasthesis and thrombocytopenia with concurrent haemoconcentration is a constant finding.

Approximately 2.5 to 3 billion people worldwide live in areas at risk for transmission of the mosquito-borne dengue flavivirus (DENV), and an estimated 100 million people worldwide are infected each year [3].

The countries with a high incidence are Indonesia, Thailand, Myanmar, Sri Lanka, Bangladesh andIndia.[4] Dengue is transmitted by mosquito *Aedes aegypti*, widely distributed throughout tropical and sub-tropical areas of the world. There are four known serotypes of dengue, but severe form of dengue fever is caused by infection by more than one serotype.[5] Clinically dengue manifests with sudden onset of high fever with chills, intense headache, muscle and joint pain, retro-orbital pain and severe backache. Fever usually lasts for about 5 days, rarely for more than 7 days.[6] Hemorrhagic diathesis and thrombocytopenia with concurrent hemoconcentration are the constant finding.

Since there is no single test that can be used to diagnose the condition with a reasonable degree of accuracy and reliability, the diagnosis is based on clinical appearance in combination with serology. Serology takes approximately 7 to 10 days to give a positive result. The purpose of our study was to analyse retrospectively the ultrasound features in patients with DF, to find out whether ultrasound is an adjunct to clinical and lab profile in the diagnosis of DF and to further determine whether ultrasound is useful in predicting the severity of the disease [7]

MATERIALS AND METHODS

The study was done in Dr. D Y Patil medical college ,tertiary care center. A cross sectional study of 100 cases who were serologically diagnosed as having dengue fever were observed from august 2015- October 2015 in our hospital and were referred for ultrasound scanning of the abdomen and thorax and the findings were analyzed.

All ultrasound examinations were performed with an ultrasound machine using 3.5 MHz and 5 MHz probes. Gallbladder (GB) wall thickening, which was the consistent finding in serologically positive cases, was measured by placing the callipers between the two layers of the anterior wall. Thoracic scanning was done in either sitting or supine posture. Both the pleural spaceswere evaluated through an intercostal approach. [8]

The serological tests for dengue including non-structural protein-1 (NS-1) Ag test and dengue immunoglobulin G / immunoglobulin M test were performed to confirm the diagnosis. NS-1, undergoes least antigenic variation and is a glycoprotein present in high concentration in the serum of dengue infected patients.

Sonographywas performed by radiologists. Scanning was performed only once so there is no inter-observer variation.

A total of 100 serologically positive patients were underwent sonography of which 75 patients had abnormal sonography report and 25 had normal report.

When we compare these dengue patients with normal ultrasonography report and abnormal report

Table 1 Comparison of patients with Normal and Abnormal ultrasonography with mean platelet and mean haematocrit

	Normal (n=25)	Abnormal (n=75)
Mean platelet (lacs)	1.2	0.716
Std Dev of platelet	0.509	0.610
Mean hct(%)	39.02	39.057
Std dev of hct	1.42	4.956

When we compare association of abnormal ultrasonography with reduced platelet count and raised haematocrit. This association was tested by t test and results as follows

Table 2 : Two sample t test for reduced platelet in patients with normal and abnormal ultrasonography findings.
Two sample Independent t test

Input Data for Platelet

Input Data for Platelet				
Two-sided confidence interval		95%		
	Sample size	Mean	Std. Dev.	Std. Error
Normal USG	25	1.2	0.509	
Abnormal USG	75	0.716	0.61	

Result	*t* statistics	*df*	p-value[1]	Mean Difference	Lower Limit	Upper Limit
Equal variance	3.57109	98	0.0005529	0.484	0.215041	0.752959
Unequal variance	3.90977	49	0.0002840	0.484	0.23523	0.73277

	F statistics	*df*(numerator,denominator)	p-value[1]
Test for equality of variance[2]	1.43623	74,24	0.3210

Table 3 : Two sample t test for raised haematocrit in patients with normal and abnormal ultrasonography findings
Two-Sample Independent t Test

Input Data forHematocrit

Input Data forHematocrit				
Two-sided confidence interval		95%		
	Sample size	Mean	Std. Dev.	Std. Error
Normal USG	25	39.02	5.823	
Abnormal USG	75	39.57	4.956	

Result	*t* statistics	*df*	p-value[1]	Mean Difference	Lower Limit	Upper Limit
Equal variance	-0.459607	98	0.6468	-0.55	-2.92475	1.82475
Unequal variance	-0.423857	36	0.6742	-0.55	-3.18168	2.08168

	*F*statistics	*df*(numerator,denominator)	p-value[1]
Test for equality of variance[2]	1.38048	24,74	0.2951

This test suggest that decrese in platelet count was associated with abnormal USG but rise in haematocrit was not associated with abnormal USG.

Out of the 100 patients, 43 had GB Wall thickness(43%), 46 had ascites (46%), 22 had bilateral pleural effusion (22%), 22 had hepatomegaly (22%), 6 had splenomegaly (6%), 42 had hepatosplenomegaly (42%) and 25 had no abnormal ultrasound findings (25%)[Table 4].

Table 4. Incidenceof different sonographic findings in dengue fever

Usg features	Numbers
Gb Wall thickness	43(43%)
Hepatosplenomegaly	42(42%)
Pleural effusion	22(22%)
Ascites	46(46%)
Hepatomegaly	22(22%)
Splenomegaly	6(6%)
Normal	25(25%)
Total number of cases	100

A total of 100 serologically positive patients were further divided into three age groups to determine the age distribution of imaging features in dengue fever. Group 1 consist of patients from 0 to 2 years (11), Group 2 had patients from 2 to 5 years of age (21), and Group 3 patients were more than 5 years of age (68).

Incidence of different sonographic findings in dengue fever
Theimportant findings regarding age distribution of imaging features are as follows:

These 100 cases further divided in 3 groups depending on their age as follows as shown in table 5. The minimum age of the patient in our study was 5 month and maximum age was 13 years.

Table 5

	<2 YEARS	2-5 YEARS	>5 YEARS
MALE	6	12	38
FEMALE	5	9	30
TOTAL	11	21	68

So, more number of dengue patients with sonological findings were in the age group of age> 5 years(n =68).

Table 6: Incidence of sonological finding in relation to age group

	0-2 years	2-5 years	>5 year
Gb Wall thickness	3	7	33
Hepatosplenomegaly	3	6	33
Pleural effusion	0	1	21
Ascites	5	7	34
Hepatomegaly	5	7	10
Splenomegaly	1	3	2
Normal	1	5	19

All the sonological finding were more in the age group of>5 years. Sonological incidence in the age group of>5 years as follows Gb Wall thickness in 33 cases, hepatosplenomegaly in 33 cases, pleural effusion in 21 cases, ascites in 34 cases, hepatomegaly in 10 cases splenomegaly in 2 cases, 19 patients were normal.

Sonological incidence in the age group of 2- 5 years as follows Gb wall thickness in 7 cases, hepatosplenomegaly in 6 cases, pleural effusion in 1 cases, ascites in 7 cases, hepatomegaly in 7 cases, splenomegaly in 3 cases, 5 patients were normal.

Sonological incidence in the age group of<2 years as follows Gb wall thickness in 3 cases, hepatosplenomegaly in 3 cases, pleural effusion in 0 cases, ascites in 5 cases, hepatomegaly in 5 cases, splenomegaly in 1case, 1 patients was normal.

The combination of imaging features observed among the groups was as follows:

GB walledemahepatosplenomegaly, ascites and pleural effusion were commonly associated with dengue fever in age group of>5 years (n =21)

Table 7: Incidence of sonographic findings in relation to different age groups

	0-2 years	2-5 years	>5 years
Ascites	1	0	3
Gb wall thickness + ascites	0	0	1
Gb wall thickness + hepatomegaly	0	2	1
Gb wall thickness + hepatosplenomegaly	0	0	5
Gb wall thickness + hepatosplenomegaly + ascites	3	3	6
Gb wall thickness + hepatosplenomegaly + ascites + bilateral pleural effusion	0	1	21
Hepatomegaly	3	3	6
Splenomegaly	1	3	2
Hepatosplenomegaly	0	1	2
Hepatomegaly + ascites	1	2	2
Hepatomegaly + ascites + gb wall thickness	0	1	1
Normal	1	5	19

Table8: Relation of various sonological combination in relation to platelet counts

	>1.5 lakhs	1.5-1 lakh	1lakh - 50000	<50000
Ascites	0	0	3	1
Gb wall thickness + ascites	0	0	0	1
Gb wall thickness + hepatomegaly	0	1	1	1
Gb wall thickness + hepatosplenomegaly	0	4	1	0
Gb wall thickness + hepatosplenomegaly + ascites	1	0	9	2
Gb wall thickness + hepatosplenomegaly + ascites + bilateral pleural effusion	0	0	6	16
Hepatomegaly	3	1	4	4
Splenomegaly	2	2	0	2
Hepatosplenomegaly	0	3	0	0
Hepatomegaly + ascites	0	2	1	2
Hepatomegaly + ascites + gb wall thickness	0	0	2	0
Normal	8	10	6	1

In this study ,the most common age group affected is> 5 years. As compared to Joshi et al which shows most common age group affected was 20-40 years but this study includedall the age group.

Table 9: Comparison of mean platelet count according to ultrasonography findings

Comparison of mean platelet count according to ultrasonography findings					
Ultrasonography findings	Obs	Total	Mean	Variance	StdDev
Normal	25.0000	31.7100	1.2684	0.2601	0.5100
Ascites	3.0000	1.4000	0.4667	0.0277	0.1665
GB wall thickness+ ascites	1.0000	0.2800	0.2800	NaN	NaN
GB wall thickness+ ascites+hepatomegaly	3.0000	1.9600	0.6533	0.0965	0.3107
GB wall thickness+hepatosplenomegaly	5.0000	4.9000	0.9800	0.0520	0.2280
GBwall thickness + hepatosplenomegaly +ascites	12.0000	8.9200	0.7433	0.2117	0.4601
GBwall thickness + hepatosplenomegaly +ascites +bilateral pleural effusion	22.0000	8.8000	0.4000	0.0426	0.2065
Hepatomegaly	12.0000	14.0900	1.1742	1.3443	1.1594
Splenomegaly	6.0000	5.9000	0.9833	0.3977	0.6306
Hepatosplenomegaly	3.0000	1.9400	0.6467	0.2380	0.4879
Hepatomegaly + ascites	5.0000	3.3900	0.6780	0.1799	0.4242
Hepatomegaly + ascites +GB wall thickness	2.0000	1.3200	0.6600	0.0072	0.0849

When we compare the dengue patients with normal ultrasonography findings & most commonly seen ultrasonography finding GB wall thickness + hepatosplenomegaly+ascites+bilateral effusion, by two sample t test and results as follows. p value for same is 0.00005429 which is statistically significant.

Table10: two sample t test for dengue patients with normal ultrasongraphy findings and with GBwall thickness + hepatosplenomegaly +ascites +bilateral pleural effusion on ultrasonography

Two-Sample Independent t Test

Input Data

Two-sided confidence interval		95%		
	Sample size	Mean	Std. Dev.	Std. Error
Normal	25	1.26	0.51	
GBwallthickness + hepatosplenomegaly +ascites +bilateral pleural effusion	22	0.4	0.2	

Result	*t* statistics	*df*	p-value[1]	Mean Difference	Lower Limit	Upper Limit
Equal variance	7.41561	45	<0.0000001	0.86	0.626421	1.09358
Unequal variance	7.77901	32	<0.0000001	0.86	0.634808	1.08519

	F statistics	*df*(numerator,denominator)	p-value[1]
Test for equality of variance[2]	6.5025	24,21	0.00005429

Which suggest that ultrasonography finding GB wall thickness + hepatosplenomegaly+ascites+bilateral effusion are associated with decreased platelet count in dengue patients.

Discussion

To our knowledge, this the first study in pediatric dengue patients which correlates with haematological reports with various ultra sonological findings. In our study , the most common age group involved is age> 5 years and ultra sonographic findings , GB wall thickness+hepatosplenomegaly+ascites+bilateral effusion were most common and seen in this age group.

When we compare this study to other studies like joshi et al[9]andV. R.Santosh et al[10], the most common age group affected is between 20-40 years.

Out of 100 cases 56 were boys and 44 were girls. Also in most common age group involved, 38 were boys and 30 were girls which shows slight preponderance for boys as shown in table no 5.

When we compare abnormal ultrasonography finding with reduced platelet count and raised haematocrit, abnormal ultra sonography correlates well with reduced platelet count. This when compared to other studies as follows. Study done in Mexican adults examined several parameters and only found association of GBWT with ascites , not thrombocytopenia (hemoconcentration was not evaluated)[11]. Balasubramanian et al [12] examined the presence of hemoconcentration in relation to ultrasonographic evidence of plasma leakage, but did not evaluate GBWT. Colbert et al study demonstrated a significant correlationof GBWT as measured by ultrasound with both thrombocytopenia and increased haematocrit, two hallmark features of severe dengue

Imaging features of dengue fever such as GB wall thickening, ascites, pleural effusion, hepatomegaly and splenomegaly are reasonably accurate in the diagnosis of dengue fever. This helps in starting appropriate management of the patient as soon as ultrasound is done, especially in centers where high end laboratory facilities may not be available for serological confirmation. While serological tests are confirmatory in the diagnosis of dengue fever, ultrasound can be of value in the assessment of severity.

Out of the 100 patients, 43 had GB wall thickness(43%), 46 had ascites (46%), 22 had bilateral pleural effusion (22%), 22 had hepatomegaly (22%), 6 had splenomegaly (6%), 42 had hepatosplenomegaly(42%) and 25 had no abnormal ultrasound findings (25%) as compared to venkatraostudy , 88 serologically positive cases, 32 patients underwent ultrasound on second to third day, repeated on fifth to seventh day of fever and in 56 patients ultrasound was done only on fifth to seventh day of fever. Of the 32 patients who underwent the study on second to third day offever, all showed gall bladder wall thickening and pericholecysticfluid, 21% had hepatomegaly, 6.25% had splenomegaly and right minimal pleural effusion. Follow-up ultrasound on fifth to seventh day revealed ascites in 53% left pleural effusion in 22% and pericardial effusion in 28%. Of the 56 patients who underwent the study on fifth to seventh day of fever for the first time all had gall bladder wall thickening, 21% had hepatomegaly, 7% had splenomegaly, 96% had ascites, 87.5% had right pleural effusion, 66% had left pleural effusion and 28.5% had pericardial fluid.

Conclusion

1. Sonographic features of thickened GB wall, pleural effusion (bilateral or right side), ascites, hepatomegaly and splenomegaly should strongly favour the diagnosis of dengue fever in patients presenting with fever and associated symptoms, particularly during an epidemic.

2. A simple ultrasound examination will effectively expedite the diagnosis and justifies initiation of specific treatment for dengue fever pending serological confirmation.

3. Ultrasound also helps substantially in estimating the severity of the disease

4. The degree of thrombocytopenia showed a significant direct relationship to abnormal ultrasound features (in various combinations) in our study

5. Ultrasound imaging features also showed a relationship to the age of the patient, most common age group affected in our study was age more than 5 years.

6. GB wall thickening, ascites and pleural effusion, hepatosplenomegaly formed the most common combination in age group of age more than 5 years.

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