Investigation on the response of young patients with dengue infection and its clinical correlation with hepatic dysfunction

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Abstract

Background and Objective: Recently, complex and unusual dengue virus infections have become a significant public health concern. Dengue may cause hepatomegaly, increased liver enzymes, and fulminant hepatic failure. To research childhood dengue hepatic dysfunction. To investigate intensity, clinical features, laboratory data, morbidity, and death.

Methods: 110 patients admitted to the Department of Paediatrics, Kamineni Institute of Medical Sciences, Narketpally, Telangana, India, due to a Dengue illness were the subjects of a prospective cohort study from March 2021 to April 2022. Patients who tested positive for the Dengue virus were chosen for further evaluation, including a complete blood count, liver function tests, abdominal ultrasound, PT, APTT, HBsAg, HCV, and Widal testing.

Result: 110 patients with dengue infection were hospitalised; 46 were diagnosed as having probable dengue, 51 as having warning signs, and 13 as having severe dengue. 42% of patients showed signs of hepatomegaly. Comparing the two groups, 88% of patients exhibited warning signals, while 100% had severe dengue. 70% of patients with probable dengue, 94% with warning signs, and 100% with severe dengue experienced thrombocytopenia. In our study, three severe dengue cases passed away. The enzyme levels were extremely high in these two cases.

Conclusion: In emerging countries like India, dengue epidemics have increased hepatic involvement to various degrees. Early detection of Dengue's temporary hepatic dysfunction could minimize life-threatening consequences. This reduces dengue morbidity and mortality. Hepatoprotective drugs should be studied for their effect on morbidity and mortality.

Keywords: Dengue, liver function, platelet count, serum bilirubin, SGPT, SGOT.

Introduction

Despite being a worldwide problem, the Indian subcontinent and other south-east Asian countries have an especially high risk of dengue fever outbreaks. Dengue fever is the only arbovirus that has reached such widespread distribution. There are at least four distinct antigenic kinds of the flaviviridae family member dengue virus, designated DEN 1, DEN 2, DEN 3, and DEN 4. Worldwide, dengue fever cases have increased dramatically during the last several decades [1, 2, 3]. Factors that contribute to the spread of dengue include population

growth, urbanization, overcrowding, inadequate health services, and an increase in travel to epidemic zones, ineffective vector control, climate change, and a lack of public awareness. The signs and severity of dengue virus infections are notoriously variable, ranging from no symptoms at all to death. Increases in the incidence of anomalies have been observed. These diseases and conditions include encephalitis, Guillain-Barre syndrome, dengue hepatitis, myocarditis, and acute respiratory distress syndrome [2, 3].

Injuries to the liver may range from mild, marked by an elevation in transaminase activity and hepatomegaly, to severe, with jaundice and fulminant hepatic failure. The severity of hepatic dysfunction may be gauged by its clinical symptoms. Several conditions, such as insufficient blood supply to the liver, metabolic acidosis, and disseminated intravascular coagulation, may lead to liver dysfunction. Consequently, this results in severe hepatic dysfunction owing to ischaemia. Dengue hepatitis should be suspected in patients who arrive with fever, jaundice, and hepatomegaly in areas where the disease is prevalent. By keeping an eye out for these symptoms, a proper diagnosis of dengue with hepatic involvement may be made more quickly, perhaps preventing more serious sequelae. But there have been few reports of studies on hepatic dysfunction in dengue. That's why we've been looking into it [4, 5, 6].

Material and Methods

A prospective cohort study was conducted on 110 patients hospitalized with dengue infection. The study was carried out by Department of Paediatrics, Kamineni Institute of Medical Sciences, Narketpally, Telangana, India, from March 2021 to April 2022. Cases who test positive for antibodies to the Dengue virus are chosen, and then they undergo a clinical evaluation to check for hepatomegaly and jaundice. In addition, these patients have a complete blood count, liver function tests, ultrasonography of the abdomen, PT, APTT, Widal, and HCV testing and analysis performed on them [6, 7].

Inclusion criteria: All cases that have had their authenticity confirmed by serology.

Exclusion criteria: Infections that are known to generate involvement of the liver, such as malaria, enteric fever, hepatitis, and leptospirosis.

Results

This research was carried out on a total of 110 individuals who tested positive for IgM dengue antibodies by serology and fell within the age range of 2 months to 12 years old. These individuals fulfilled the WHO criteria for the diagnosis of dengue infection.

Table 1: Diagnosis

Diagnosis	Frequency	Percent
Probable dengue (pd)	46	42
Dengue with waarning signs (d+ws)	51	46
Severe dengue (sd)	13	12
Total	110	110

There were 110 people admitted to the hospital with a dengue infection. Of those patients, 46 were diagnosed as having a dengue infection that was Probable, 51 were diagnosed as having Warning Signs, and 13 were suffering from Severe Dengue.

Table 2: Age distribution of patients

Age in yrs.	Diagnosis PD	Diagnosis D+SD	Diagnosis SD	Total
1	1	1	-	2
2	5	5	-	10
3	1	7	5	13
4	7	8	-	15
5	4	9	2	15
6	8	4	1	13
7	4	2	2	8
8	3	6	2	11
9	3	3	-	6
10	7	1	-	8
11	3	-	1	4
12	-	5	-	5
Total	46	51	13	110

Dengue mainly affected children of age group 5 to 7 years.

Table 3: Gender distribution of cases

Diagnosis	Gender of the child Male N	Male %	Female N	Female %	Total
PD	27	58.69	19	41.30	46
D+WS	29	56.86	22	43.13	51
SD	6	46.15	7	53.84	13
Total	62	56.36	48	43.63	110

Dengue affected male and female children almost equally.

Table 4: Comparison of changes in liver function tests and platelet count

	Normal N	Normal %	Decreased N	Decreased %	Increased N	Increased %	Total
Platelet	17	15	93	88	-	-	110
Sbr-total	95	86	-	-	15	10	110
Sgot	31	28	-	-	79	74	110
Sgpt	47	43	-	-	63	58	110
Alp	77	70	-	-	33	28	110
Pt	94	85	-	-	16	11	110
Aptt	94	85	-	-	16	11	110
S. Protein	93	84	17	12	-	-	110
Albumin	102	92	8	7	-	-	110

Table 5: Comparison between groups with respect to hepatomegaly

Liver span	Diagnosis PD	Diagnosis D+WS	Diagnosis SD	Chi square	p
Normal	46	6		88.65	0.001**
Increased	0	45	13		
Total	46	51	13		

Hepatomegaly was seen in 42% of participants throughout this study. When the two groups were compared, there was a difference of 88% in patients who had warning signals and 100% in those who had encountered severe dengue.

Table 6: Comparison between groups with respect to platelet count

Platelet	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	14	30	3	6	-	-	17	13.85	0.001**
Decreased	32	70	48	94	13	100.0	93		
Total	46	100.0	51	100.0	13	100.0	110	-	-

** Significant at 1% (Highly significant)

70% of patients with probable dengue had thrombocytopenia, 94% of patients with warning symptoms, and 100% of patients with severe dengue had thrombocytopenia.

Table 7: Comparison between groups with respect to serum bilirubin

Sbr- total	Diagnosis						Total	Chi square	P
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	46	100.0	51	100.0	1	7.7	98	89.90	< 0.001**
Increased	-	-	-	-	12	92.3	12		
Total	46	100.0	51	100.0	13	100.0	110		

** Significant at 1% (Highly significant)

Twelve of the individuals in this research had a severe case of dengue fever, and all of them had elevated blood total bilirubin levels.

Table 8: Comparison between groups with respect to serum SGOT

SGOT	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	19	41.4	11	21.5	-	-	30	9.59	0.008**
Increased	27	58.6	40	78.4	13	100.0	80		
Total	46	100.0	51	100.0	13	100.0	110		

** Significant at 1% (Highly significant)

Eighty percent of dengue patients had an elevated level of SGOT in their serum. A spike in SGOT was shown to have occurred in 58.6% of patients with probable dengue, 78.4% of patients with warning symptoms, and 100% of patients with severe dengue when all three groups were compared.

Table 9: Comparison between groups with respect to serum SGPT

SGPT	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	26	56.5	18	35.3	3	23	47	7.74	0.021*
Increased	20	43.5	33	64.7	10	77	63		
Total	46	100.0	51	100.0	13	100.0	110		

* Significant at 5%

In 30% of individuals with dengue infection, there was an elevation in SGPT. A spike in SGPT was seen in 13% of patients with probable dengue, 33.4% of patients with warning symptoms, and 76.9% of patients with severe dengue when all three groups were compared against one another.

Table 10: Comparison between groups with respect to serum alkaline phosphatase

ALP	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	40	87	34	66.6	3	23.1	77	23.27	< 0.001**
Increased	6	13	17	33.4	10	76.9	33		
Total	46	100.0	51	100.0	13	100.0	110		

** Significant at 1% (Highly significant)

In 58% of individuals with dengue infection, an elevated level of serum alkaline phosphatase was seen. A spike in SGPT was seen in 9.5% of patients with probable dengue, 32.0% of patients with warning symptoms, and 82.0% of patients with severe dengue when all three groups were contrasted against one another.

Table 11: Comparison between groups with respect to serum alkaline phosphatase

PT	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	46	100.0	46	90.2	4	30.7	96	49.03	< 0.001**
Increased	-	-	5	9.8	9	69.3	14		
Total	46	100.0	51	100.0	13	100.0	110		

** Significant at 1% (Highly significant)

In individuals with dengue infection, an increased prothrombin time was seen in 14% of cases. A spike in PT was seen in 9.8% of patients with warning symptoms and in 69% of patients with severe dengue when the two groups were compared.

Table 12: Comparison between groups with respect to APTT

APTT	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	46	100.0	46	90.2	4	30.7	96	49.03	< 0.001**
Increased	-	-	5	9.8	9	69.3	14		
Total	46	100.0	51	100.0	13	100.0	110		

** Significant at 1% (Highly significant)

In individuals who had dengue infection, an increased Activated Partial Thromboplastin Time was seen in 14% of cases. When the two groups were compared, we found that a spike in APTT occurred in 9.8% of patients with warning symptoms and in 69.3% of patients with severe dengue.

Table 13: Comparison between groups with respect to serum total protein

S. Protein	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	46	100.0	43	84.4	6	46.1	95	24.61	< 0.001**
Decreased	-	-	8	15.6	7	53.8	15		
Total	46	100.0	51	100.0	13	100.0	110		

** Significant at 1% (Highly significant)

In 15% of individuals with dengue illness, there was a decrease in the total protein content of the serum. When looking at the difference in blood protein levels between the two groups, we

found that 15.6% of people with warning signals had it, whereas 53.8% of those with severe dengue had it.

Table 14: Comparison between groups with respect to serum albumin

Albumin	Diagnosis						Total	Chi square	p
	PD		D+WS		SD				
	N	%	N	%	N	%			
Normal	46	100.0	47	92	11	85	104	2.96	0.228
Decreased	-	-	4	8	2	5	6		
Total	46	100.0	51	100.0	13	100.0	110		

Albumin levels in the patients' serum were lower in 6% of cases with dengue infection. When looking at the difference in serum albumin levels between the two groups, we found that 8% of those with warning symptoms and 5% of those with severe dengue had it.

Table 15: Outcomes

Outcome	Diagnosis			Total	Chi square	p
	PD	D+WS	SD			
Expired	-	-	3	3	16.51	< 0.001**
Recovered	46	51	10	107		
Total	46	51	13	110		

** Significant at 1% (Highly significant)

In the course of our research, three patients who were severely affected by dengue fever passed away. In each of these instances, the levels of enzymes were significantly elevated.

Discussion

Dengue fever is among the most dangerous of the infectious illnesses that may be transmitted by mosquitoes. The dengue virus, which is responsible for dengue fever, has four basic serotypes: DEN 1, DEN 2, DEN 3, and DEN 4. Dengue fever is caused by the dengue virus. Its symptoms cover a broad range, ranging from being asymptomatic to having the potential to be lethal. According to the most current data, the frequency of this disease among children seems to be on the increase [8, 9].

74% of patients diagnosed with dengue showed hepatic involvement, which was characterized as hepatomegaly in the study by Luiz Jose de Souza *et al*. In the study by Nimmantya *et al*., the success rate was 98%, whereas in the study by Gurdeep S. Dhoria *et al*., it was only 60%. In Ole Wichmann and colleagues' study, the prevalence of hepatomegaly was found to be 43%, but in Brij Mohan and colleagues' study, it was 74%. 74% according to kuo *et al*., and 55% according to the findings being presented here [9, 10].

Hepatomegaly was more likely to be present in patients who had moderate to severe dengue as well as those who had previously shown warning signs. In the present study, hepatomegaly was found in 55% of participants who were diagnosed with probable dengue, in% of participants who were diagnosed with dengue fever, and in% of participants who were diagnosed with severe dengue fever [10, 11].

Therefore, hepatomegaly may be used as a method for determining the severity of the condition. It is possible that the pace of rise in liver enzymes might serve as a measure of how severe the illness is. The prognosis is not encouraging if liver enzyme levels are elevated. The researchers Brij Mohan and colleagues found that the levels of both SGOT and SGPT increased during the course of the first week of the investigation, respectively. By the third week, both had begun to show signs of improvement. One further enzyme that was shown to be rising in levels was serum alkaline phosphatase. According to Nimmannitya *et al*., SGOT levels began to increase on day 3, reached a peak on day 7, then recovered to normal after

about three weeks of treatment. Given that hepatocytes are the cells to which SGPT is most directly associated, an increase in this enzyme's activity after damage to the liver makes perfect sense. A rise in SGPT levels is caused by damage to cardiac and skeletal muscle as well as hepatocytes, renal, and brain tissue. During the acute febrile phase of dengue infection, an increase in liver enzyme levels may be able to be observed [11, 12].

Seventy-four percent of those who had dengue had abnormally high levels of SGOT in their blood. 74% of patients with probable dengue had an increase in their SGOT, as did 98% of patients with warning signs, and 100% of patients with severe dengue had an increase in their SGOT.

In their respective studies, M Narayanan and colleagues, Srivenu Itha and colleagues, and Brij Mohan and colleagues all discovered anomalies in the levels of liver enzymes. According to the findings of Souza *et al*. and Kuo *et al*., respectively, in 63.4% of all cases and 97.9% of all occurrences [12, 13].

A high level of SGPT was found in five-eighths of dengue patients. 42% of patients with probable dengue had an increase in their SGPT, whereas 66% of patients with warning signs and 81% of patients with severe dengue had an increase in their SGPT. In addition to the research that was just described, which was conducted by M. Narayanan and colleagues, SrivenuItha *et al*. and Brij Mohan *et al*. also discovered a rise in SGPT. Luiz Jose Souza and colleagues reported a rise in ALT levels in 45% of their patients. It was discovered that the levels of ALT had grown in 82% of the people whom Kuo and colleagues researched. According to the findings of MMA Faridi *et al*., the levels of ALT rose by 64.6%. There was a connection between patients' higher enzyme levels and the degree to which they were affected by dengue fever [14, 15, 16].

Patients diagnosed with dengue fever exhibited an increased alkaline phosphatase level in proportion to two-eighths of the total (SGPT). An elevation in SGOT was seen in 9.5% of patients with probable dengue, 32% of patients with warning signs, and 82% of patients with severe dengue. According to the ALP investigations conducted by Kuo *et al*., the elevation gained was 16%. 35.3 percentage points for Faridi *et al*. The most recent investigation reaches a height of 28%.

The manifestation of jaundice is suggestive of a grim outlook on the patient's health. There is a correlation between chronic hepatitis and acute liver failure. This analysis found that 10% of the persons who had severe dengue disease were found to have excessively high amounts of total bilirubin in their blood [17, 18].

Hypoalbuminemia is a measurement of the quantity of albumin that is present in the blood and may arise as a consequence of liver injury and capillary leakage. In the current research, there was a case of hypoalbuminemia found in 12% of the subjects. 16.5% of the people who participated in the research that Manzhi Wong and his colleagues did had hypoalbuminemia, as shown by the findings of the study.

The length of prothrombin time is determined by clotting components that are vitamin K dependent [17, 18].

A PT anomaly is often shown to be connected with more severe instances of dengue fever. According to these findings, 11% of dengue patients had an elevated prothrombin time. An increase in PT was seen in 6.4% of people with moderate dengue symptoms and 72.0% of those with severe dengue symptoms. Researchers from Sri Venutha and colleagues discovered that the PT was extended in 16% of individuals.

Patients with dengue fever were more likely to have an increased Activated Partial Thromboplastin Time (11%), while 6.4% of patients with warning symptoms and 72% of patients with severe dengue had an increase in APTT. In raised activated partial thromboplastin time in patients with dengue fever were more likely to have an increased APTT. 74% of those who had probable dengue were impacted by thrombocytopenia, whereas 98% of those who had moderate symptoms and 100% of those who had severe dengue were afflicted by thrombocytopenia [19, 20].

There were 110 individuals hospitalized with dengue who had their diagnoses confirmed by

serology. Of the 110 patients, 42 were diagnosed as possibly having dengue, 47 were diagnosed with having warning signs of dengue, and 11 were diagnosed with having severe dengue. Two patients who had severe dengue fever ultimately passed away as a result of DIC. There was a very high increase in the levels of enzymes [20].

Conclusion

There has been an increase in the number of cases of dengue fever that have been reported in developing nations such as India. Hepatic involvement of varying degrees have been documented. Early discovery of the problem would help to decrease the danger of life-threatening outcomes, since the hepatic dysfunction that is produced by dengue is only transient and may be reversed. Because of this, there is a possibility that the mortality and morbidity rates linked with dengue infection might be reduced. It is necessary to conduct further studies in order to examine and comprehend the role that hepatoprotective drugs play in reducing the rates of morbidity and mortality.

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