

# Study of Pulmonary Manifestations among Dengue Patients in Tertiary Care Hospital of North India

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## ABSTRACT

**Introduction:** Thoracic manifestations such as pleural effusion, pneumonia, and haemoptysis have been reported in dengue infection. Dengue haemorrhagic fever (DHF) can result in acute respiratory distress syndrome. Dengue shock syndrome (DSS) is reported to be the third leading cause of ARDs in dengue endemic area. Current research aimed to study pulmonary manifestations among dengue hospitalized patients.

**Material and Methods:** This study was conducted in 50 patients of dengue confirmed by dengue serology. Respiratory manifestations were recorded and all clinical examination findings were recovered. Baseline investigations including complete blood count, liver profile, renal profile, arterial blood gas analysis, dengue virus IgM and IgG and ns1 antigen, chest x-ray, ultrasound thorax and abdomen ultrasonography were done.

**Results:** Young age patients and patients with co-morbidity are risky to severe form of dengue fever and have a high risk of death. As regards co-morbidities, chronic chest disease and cardiac disease are mostly vulnerable to Dengue Haemorrhagic Fever and Dengue Shock Syndrome. The most presenting respiratory manifestations were Acute Respiratory Distress Syndrome followed by pneumonitis and pleural effusion.

**Conclusion:** Incidence of pulmonary complications among cases of Dengue is quite high and therefore can be used as an indicator of serious presentation of dengue in the patients.

**Keywords:** Dengue, Acute Respiratory Distress Syndrome, Pneumonia, Pleural effusion, Dengue Hemorrhagic Fever, Dengue Shock Syndrome

## INTRODUCTION

One of the commonest arboviral infections in human is Dengue fever caused by flavivirus infected *Aedes* mosquitoes.<sup>1,2</sup> Around 50 million dengue infections are reported annually with 5 million cases of severe dengue in form of Dengue Haemorrhagic Fever (DHF) with annual mortality of 12,000.<sup>3</sup> Highest incidence of dengue epidemic has been found in the South American countries, south-east Asian countries and Africa. Data on dengue infections are substantially high in 2019 as compared with the same period in 2018 because of simultaneous circulation of all the four dengue virus serotypes (DENV 1, DENV 2, DENV 3, and DENV 4), which increases the risk of severe cases.<sup>4</sup> Rapid risk assessment and management programmes have been issued since the dengue epidemic is internationally an important public health problem.<sup>4,5</sup> Although dengue is self-limiting but complications like Dengue shock syndrome

(DSS) and DHF can be very life-threatening. Mortality from these complications is 20% or even higher in the low to middle income countries (LMICs). Apart from the classical clinical features of dengue some atypical presentation can be seen in clinical practice.<sup>6</sup> One of which is respiratory presentation of dengue which is very commonly caused by the immune pathological mechanisms involved in the dengue fever (DF).<sup>7</sup> Acute respiratory distress syndrome (ARDS) can be caused by DF through mechanisms with systemic involvement. Increased vascular permeability of the alveolar-capillary membranes results in oedema in the alveoli and interstitial spaces thus leading to pulmonary dysfunction and coagulation disorders.<sup>7,8,9</sup> Other leading cause of ARDS is DSS and pleural effusion.<sup>10</sup> In the pathogenesis of dengue, pleural effusion and pulmonary edema also consistent with DF. Pleural effusion due to plasma leakage is presented in about 38.6% of the severe dengue cases.<sup>11</sup> Disturbance of colloid oncotic pressure could possibly be the cause of pulmonary edema presented in many dengue cases.<sup>12</sup> Therefore this research aims to study pulmonary manifestations among dengue hospitalized patients.

## MATERIAL AND METHODS

The study included 50 dengue patients, confirmed by NS 1 ANTIGEN admitted to teaching hospital of North India. Patients were recruited from the Intensive Care Unit (ICU) and respiratory medicine ward from July 2019 to October 2019. Patients were screened by physical examination and full clinical history. Dengue fever was clinically suspected on the basis of presence of febrile illness, headache, low platelet, myalgia, retro-orbital pain, bleeding, haemoptysis, shock, cough, dyspnoea and chest pain. Informed consent was taken from all the eligible patients or their family members who volunteered to be a part of the study. Demographics data was collected along with the clinical parameters and investigations which included complete blood count (CBC),

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haematocrit, renal profile, liver profile and arterial blood gas analysis (ABG). Serological testing: Sera were evaluated by indirect IgG ELISA to inactivated dengue virus, IgM antibody capture ELISA (MACELISA) produced in tissue culture and nS1 antigen. Chest X-ray P.A view and USG thorax were done. All respiratory manifestations in the patients were also recorded.

Data was collected and analysed by using Stata version 15. Continuous variables were represented as mean (SD) and categorical variables were represented as frequency (%). Inferential statistics was performed using independent t-test for continuous outcomes and Chi-squared test or Fishers exact test for categorical outcomes, considering p value <0.05 for statistically significance.

## RESULTS

There were 50 cases of dengue, recruited from the ICU and respiratory medicine wards from July 2019 to October 2019. Table 1 shows the demographic profile of all the dengue patients in terms of gender, age, residence, socio-economic and lifestyle factors and its association with mortality in such cases. There is statistically significant association between mortality due to dengue with age, residence socio-economic status and lifestyle factors like smoking, alcohol consumption and tobacco consumption of the patient. Mortality is high in the younger age group (age less than 30 years) as compared

to older age group (age 30 -50 years and more than 50 years). Figure 1 shows the age distribution of all dengue cases. The study had higher proportions of the young age group less than 30 years of age. Moreover patients belonging to rural setting with low socio-economic have higher mortality because of dengue. Lifestyle factors like smoking, consuming alcohol and tobacco increases dengue mortality, as shown in Table 1. Demographics of the patients reveal that the dengue presented clinically as dengue fever in 20 patients with 11.1% mortality, dengue haemorrhage fever (DHF) in 22 patients with 59.2% mortality and Dengue shock Syndrome

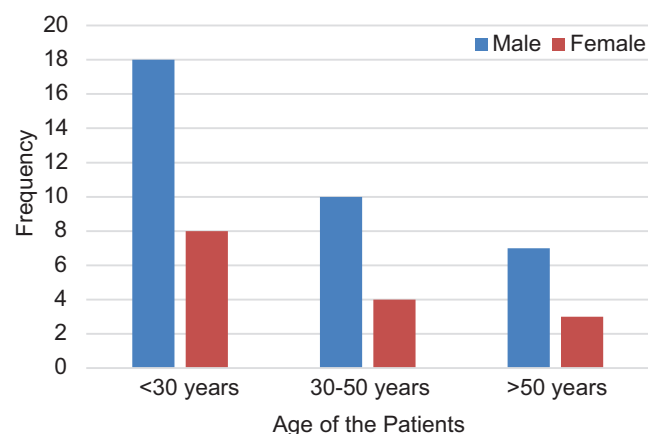


Figure-1: Age distribution of dengue cases

Characteristics	Cured cases		Dead cases		Total	p- value
	(n= 23)	%	(n=27)	%		
Gender						
Male	15	65.3	20	74.1	35	0.144
Female	8	34.7	7	25.9	15	
Age						
<30 years	11	48.0	15	55.5	26	0.025*
30-50 years	6	26.0	8	29.6	14	
>50 years	6	26.0	4	14.9	10	
Residence						
Urban	8	34.7	10	37.0	18	0.012*
Rural	15	65.3	17	63.0	32	
Socio-Economic						
Upper class	2	8.7	0	0.0	2	0.043*
Upper middle class	8	34.7	8	29.6	16	
Lower middle class	10	43.5	13	48.1	23	
Lower class	3	13.1	6	22.3	9	
Lifestyle						
Smoking	1	4.3	6	22.3	7	0.027*
Alcohol	4	17.4	5	18.5	9	0.034*
Tobacco	3	13.0	10	37.0	13	0.042*

\*Statistically significant p-value >0.05

Table-1: Demographic profile of the hospitalised dengue patients

Clinical presentation	Cured cases		Dead cases		Total	p- value
	(n= 23)	%	(n=27)	%		
Dengue fever (DF)	17	73.9	3	11.1	20	<0.001*
Dengue haemorrhage fever (DHF)	6	26.1	16	59.2	22	<0.001*
Dengue shock syndrome (DSS)	0	0.0	8	29.7	8	<0.001*

\*Statistically significant p-value >0.05

Table-2: Clinical profile of dengue illness

(DSS) in 8 patients with 100% mortality, as shown in Table 2. Higher mortality is associated with severe forms of dengue that is DHF and DSS. Table 3 shows the distribution of co-morbidities among the different clinical presentations

of dengue. Patients with higher co-morbidities like diabetes, hypertension, cardiac diseases and chronic chest diseases showed severe forms of dengue such as Dengue haemorrhage fever and Dengue shock syndrome, therefore

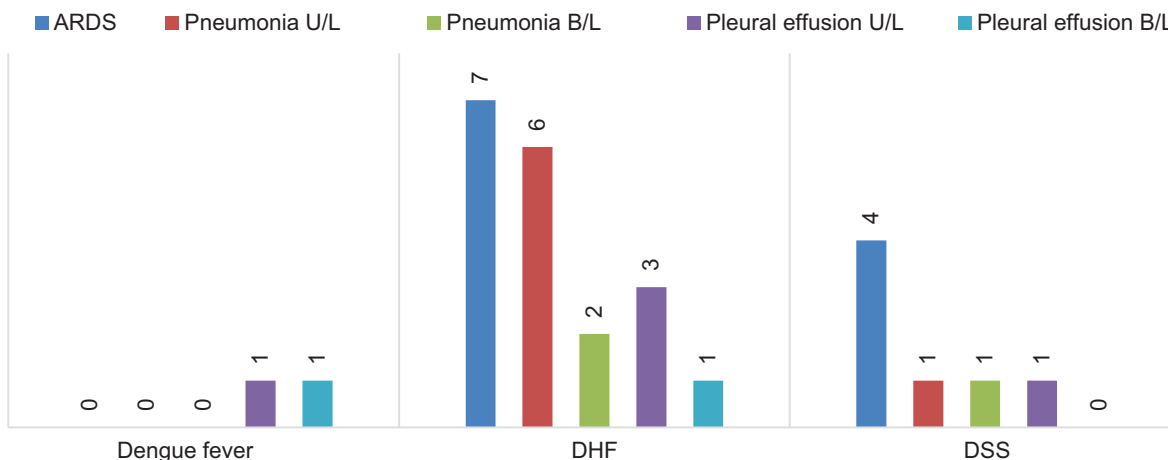


Figure-2: Pulmonary manifestations in dengue cases

Co-morbidity	Dengue fever		DHF		DSS	
	(n= 20)	%	(n=22)	%	(n=8)	%
Diabetes	0	0.0	1	4.5	1	12.5
Hypertension	0	0.0	1	4.5	0	0.0
Chronic kidney disease	0	0.0	0	0.0	1	12.5
Chronic hepatic disease	0	0.0	0	0.0	1	12.5
Cardiac disease	0	0.0	3	13.6	1	12.5
Chronic chest disease	0	0.0	3	13.6	4	50.0

Table-3: Co- morbidities presented in the different clinical presentations of dengue

Pulmonary manifestations	Dengue fever		DHF		DSS		Total (n=50)	p-value
	(n= 20)	%	(n=22)	%	(n=8)	%		
ARDS	0	0.0	7	31.8	4	50.0	11(22%)	0.025*
Pneumonia								
U/l	0	0.0	6	27.3	1	12.5	7(14%)	0.81
B/l	0	0.0	2	9.1	1	12.5	3(6.0%)	0.24
Pleural effusion								
U/l	1	5.0	3	13.6	1	12.5	5(10.0%)	0.37
B/l	1	5.0	1	4.5	0	0.0	2(4.0%)	0.29
Total	2	10.0	19	86.4	7	87.5	28(56%)	0.001*

\*Statistically significant p-value >0.05

Table-4: Pulmonary manifestations in different clinical presentations of dengue

Clinical symptoms	Dengue cases with pulmonary complications		Dengue cases without pulmonary complications		Total (n=50)	p- value
	(n= 28)	%	(n=22)	%		
Fever	28	100.0	22	100.0	50	>0.999
Cough	22	78.6	12	54.5	34	0.012*
Body pain	28	100.0	22	100.0	50	>0.999
Vomiting	5	17.8	7	31.8	12	0.025*
Dyspnoea	26	92.8	2	9.0	28	0.001*
Haemoptysis	13	46.4	2	9.0	15	0.033*
Drowsiness	7	25.0	11	50.0	18	0.092
Shock	23	82.1	11	50.0	34	0.032*
Bleeding from other site	7	25.0	1	4.5	8	0.045*

\*Statistically significant p-value >0.05

Table-5: Clinical profile of dengue cases developing pulmonary complications

having higher mortality. Most common co-morbidities were cardiac disease and chronic chest disease in the cases with DHF and DSS. Table 4 shows pulmonary manifestations like acute respiratory distress syndrome (ARDS), pneumonia and pleural effusion were more common in the severe cases of dengue as compared to dengue fever, with significant p-values.

ARDS (11 cases) was the most common form of pulmonary manifestation followed by pneumonia (10 cases) and pleural effusion (7 cases), in all dengue cases. In all the 22 dengue cases with DHF, 31.8% cases had ARDS, 36.4% had pneumonia and 18.1% had pleural effusion. Similarly there was high prevalence of ARDS (50%) among total 8 cases of DSS, followed by 25% cases of pneumonia and 12.5% cases of pleural effusion. Pulmonary complications were seen in only 10% patients of the non-complicated cases of dengue as pleural effusion. Table 5 compares the clinical profile among cases with pulmonary complications and without pulmonary complications. Although fever and body pain were observed in all the patients irrespective of pulmonary complications, but other clinical symptoms like cough ( $p=0.012$ ), dyspnoea ( $p=0.001$ ), haemoptysis ( $p=0.033$ ), shock ( $p=0.032$ ) and bleeding from other sites ( $p=0.045$ ) are markedly presented in dengue cases with pulmonary complications as compared with cases without pulmonary complications, with statistically significant p values. In dengue cases developing pulmonary complications ( $n=28$ ), clinical presentations of symptoms like cough was 78.6% and haemoptysis was 32.1%. Other symptoms were fever (100.0%), body pain (100.0%), vomiting (17.8%), dyspnoea (92.8%), drowsiness (25%), shock (82.1%) and bleeding from other sites (25%).

## DISCUSSION

Pulmonary manifestations are often reported in the severe cases of dengue. Pleural effusions, acute respiratory distress syndrome (ARDS), pneumonitis and haemoptysis can be caused by the dengue haemorrhagic fever. Among all the causes of ARDS, dengue shock syndrome is one of the major causes. Similar results are reported by Guzman, showing lung pathology in all fatal dengue cases, and the presence of the virus in the lungs of the dead cases.<sup>13</sup> Reports from Venezuela also showed the same finding, lung diseases (non-cardiogenic pulmonary oedema, diffuse alveolar damage, thromboembolism, bronchopneumonia, pneumonitis, haemorrhage) were cause of death in two-thirds of dengue death cases.<sup>14</sup> Report from Yunnan showed that 38.6% of severe dengue cases presented pleural effusion due to plasma leakage.<sup>15</sup> In this study out of 50 dengue patients, 20 dengue fever cases, 22 dengue haemorrhagic fever cases, and 8 dengue shock syndrome cases. Table 1 shows a statistically significant high mortality due to dengue in the age group of less than 30 years as compared to higher age groups. Table 2 shows the statistically significant association of higher mortality with the severe cases of dengue like DHF and DSS. These results can be explained by the fact that young patients who are at higher risk of severe complications, are also at high risk of acquiring severe forms of dengue

disease, resulting in higher mortality. This is shown in Table 3, that patients with co-morbidities have a high death rate than those who don't have co-morbidities. These results are concomitant with Sameer et al, who showed DHF is often characterised by haemorrhages and shock syndrome which is fatal.<sup>7</sup> This is mostly because of the severe infection and increased virus production in other organs like liver and bone marrow. Fluid from blood stream leaks through the wall of small blood vessels inside the body's cavities. This results in less blood circulation in the blood vessels and low blood pressure, therefore deficiency of oxygen to the vital organs. Table 4 shows different pulmonary manifestations in the patients. There was statistically significant difference in the prevalence of pulmonary manifestations in the severe cases of dengue as compared to mild dengue. These were presented as ARDS, haemoptysis, pneumonitis unilateral and bilateral, and pleural effusion unilateral and bilateral in the cases of DHF and DSS. These results can be explained by the fact that dengue virus antigen is found in the alveolar lining of lungs and the increased alveolar permeability, results in oedema in the lung cavities which cause pulmonary dysfunction. Many studies have reported ARDS in the DHF cases.

Table 5 presents clinical symptoms like fever, body ache and headache in all the dengue cases irrespective of presence of pulmonary complications. Whereas there was a significant increase of clinical symptoms like shock, haemoptysis, bleeding from other sites and drowsiness among dengue patients with pulmonary complications compared to those without pulmonary complications. This might happen because of the increased risk of lung complications in the severe cases of dengue having higher mortality. Through previous literature as well as this study we find that respiratory complications could be an indicator to check the severe forms of dengue. However due to a small sample size, these results need further investigation for confirmation.

## CONCLUSION

Incidence of pulmonary complications in the serious cases of dengue like DHF and DSS is quite high as compared to less severe forms of dengue. Therefore can be used as an indicator of serious presentation of dengue in the patients.

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