The value of lung involvement in recognizing severe dengue-A retrospective study

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Abstract

Background Dengue fever is a vector-borne disease transmitted by infected female Aedes mosquitoes. It has become the major threat to human beings especially in tropical and subtropical areas. It's important to find early parameters to identify severe dengue due to its poor prognosis. This study aimed to explore the value of lung involvement in identifying severe dengue (SD) from ordinary dengue.

Methods 592 dengue patients admitted in the Third Affiliated Hospital of Sun Yat-sen University from July 2014 to January 2020 were enrolled. Patients were divided into two groups, dengue with lung involvement group (DWLI) and dengue without lung involvement group (DWOLI). According to the severity of dengue fever, patients in DWLI group were further divided into dengue subgroup and SD subgroup. The clinical characteristics, treatment and outcome of the patients were analyzed between groups and subgroups respectively.

Results The rate of SD patients was higher in DWLI group than that in DWOLI group. The ratios of old age, smoking, hepatobiliary disease, hypertension, diabetes, coronary heart disease and cerebrovascular disease were higher in DWLI group than those in DWOLI group (all $p<0.05$). Other organs such as liver, kidney, digestive tract were affected more in DWLI group (all $p<0.05$). Respiratory symptoms such as cough and breathlessness were more common in DWLI group (both $p<0.05$). Subgroup analyses showed that SD subgroup patients had more respiratory symptoms as well ($p<0.05$). Inflammatory markers including C-reactive protein (CRP) and pro-calcitonin (PCT) were increased in DWLI group (both $p<0.05$). The ratios of pleural effusion and bilateral lung infiltration were correlated with SD (both $p<0.05$). The ratios of anti-virus□anti-bacteria and combined therapy were higher in DWLI group. There were 10 cases in DWLI group complicated with multiple organ dysfunction syndrome (MODS) while no MODS occurred in DWOLI group. Except for 2 patients with MODS died, all the other patients were cured.

Conclusions Among dengue fever patients, the elderly, smoking population, those accompanied by underlying diseases were prone to have lung involvement. Dengue fever patients who develop clinical manifestations such as cough, breathlessness, pleural effusion and bilateral pneumonic exudation should be warned of SD.

Background

Dengue fever is a vector-borne disease transmitted by infected female Aedes mosquitoes. It is single-stranded positive-sense RNA virus belonging to the genus Flavivirus with four serotypes [1]. Among the infectious diseases, dengue has become the major threat to human beings especially in tropical and subtropical areas. In recent decades, the infection is increasing year by year around the world. The disease have impacted more than 120 countries, there are about 3.9 billion people at risk of getting infection of dengue virus. It is estimated that the annual incidence is about 390 million globally, including 96 million with apparent manifestations. The disease burden of dengue was up to 25.5 disability-adjusted life years per 100,000 population [2, 3]. Dengue virus can cause various symptoms and signs

despite most of the cases are asymptomatic. According to the severity of the disease, it can be divided into two types, dengue (with/without warning signs) and severe dengue (SD). The requirements to reach a diagnosis of SD are: severe bleeding, severe organ impairment or dengue shock [4].

Respiratory symptoms used to be considered not very common in dengue patients. Those reported clinical respiratory features were mild or only affecting upper airway, whereas severe involvement of the lower respiratory airway was rarely seen [5, 6]. However, it has arisen more attention as the spreading use of imaging technologies such as X-ray and computerized tomography (CT) in these years. Pleural effusion, pulmonary hemorrhage, pneumonia can be seen especially in SD patients with severe plasma leakage and lead to dyspnea [7]. There are few studies exploring the relationship between pulmonary involvement and SD. In order to improve the capacity of managing dengue and SD with lung involvement among medical staff, we conducted this retrospective study enrolling dengue and SD admitted in our hospital.

Methods

Study design

592 confirmed cases of dengue fever admitted to the Third Affiliated Hospital of Sun Yat-sen University from July 2014 to January 2020 were enrolled in the study. The informed consent to use the test results for medical research were obtained from the patients. This study conformed to the ethics principles of the Declaration of Helsinki and Good Clinical Practice and to the regulatory requirements of China. It also obtained ethical approval from the Institutional Review Board (IRB) of the Third Affiliated Hospital of Sun Yat-Sen University ([2019]02-459-01).

The diagnostic criteria of dengue and severe dengue conformed to the guidelines for diagnosis and treatment of dengue (2014 version, and 2018 version) [8, 9]. For those who were diagnosed as suspected or clinical cases of dengue fever according to epidemiological history and clinical manifestations, if they met one of the following two criteria, they were diagnosed as confirmed case: 1. Non-structural protein 1 (NS1) was positive; 2. Viral nucleic acid polymerase chain reaction (PCR) was positive.

Based on whether there was lung involvement, the confirmed patients were divided into two groups as dengue with lung involvement (DWLI) and dengue without lung involvement (DWOLI). DWLI had any of the following characteristics: 1. Obvious aggravation of cough or breathlessness; 2. Hemoptysis; 3. New signs or changes in pulmonary imaging. Those with cough, breathlessness, diffused patchy changes in the lungs caused by acute heart failure were excluded. There were 213 patients in DWLI group and 379 in DWOLI group.

In DWLI group, 213 cases were further divided into two subgroups, dengue subgroup containing 91 cases and SD subgroup with 122 cases. SD was diagnosed if patients reached one of the following conditions: 1. Severe bleeding (including subcutaneous hematoma, hematemesis, black stool, vaginal bleeding, gross hematuria, intracranial hemorrhage, etc.); 2. Shock (including tachycardia, limb dampness, weak or

undetectable pulse, decreased pulse pressure or undetectable blood pressure); 3. Severe organ damage (including liver injury, acute respiratory distress syndrome, acute myocarditis, acute renal failure, encephalopathy or encephalitis).

Laboratory test

Common laboratory tests and chest imaging were performed by the department of laboratory and image center of the Third Affiliated Hospital of Sun Yat-sen University. Dengue virus nucleic acid was detected by PCR technology in Guangzhou Center for Disease Control and Prevention.

Statistical analyses

Continuous variables were described as means and standard deviations (Mean ±SD or median and quartile intervals were P_{50} (P_{25}-P_{75}). Categorical variables (*e.g.* age and gender) were described as numbers and percentages. For variables such as age, heat peak, common test results, since they did not conform to normal distribution and variance is uneven, rank sum test was used. The counting data was tested by Pearson chi square or Fisher accurate test. $P<0.05$ was considered statistically different. All statistical analyses were performed using IBM SPSS Statistics Version 20 (Chicago, USA).

Results

General characteristic

The ratio of SD in DWLI group was 57.3% (122/213), significantly higher than 23.7% (90/379) in DWOLI group ($p<0.05$). In DWLI group, the ratio of male to female was 1.48:1 (127/86). In DWOLI group, the ratio was 1.26:1 (211/168). The gender ratio between the two groups was close without statistical difference ($p>0.05$). The median age of the patients in DWLI and DWOLI groups were 53 and 32 years, respectively. The proportion of patients over 65 years old was 29.58% (63/213) and 6.07% (23/379), respectively. The median age and proportion of elderly patients in the DWLI group were significantly higher than those of DWOLI group (both $p<0.05$). The proportion of smoking population was 20.66% (44/213) in DWLI group, significantly higher than 11.35% (43/379) in DWOLI group ($p<0.05$). The most common underlying diseases in all cases included hepatobiliary disease, hypertension, diabetes, coronary heart disease and cerebrovascular disease, whose proportion were significantly higher in DWLI group (Table 1).

Clinical manifestation

The median onset time were 5 days in both DWLI and DWOLI groups. The most common clinical symptoms in both groups were fever. Except for 2 cases in the DWLI group, all of the other patients had fever, with the median thermal spike of 39.0 ℃ in both groups. There were no hemoptysis in both groups. The ratio of multiple organ dysfunction syndrome (MODS) in DWLI group was 4.7% (10/213), significantly higher than 0 (0/379) in DWOLI group ($p<0.05$). The kidney injury was more frequent in DWLI group than DWOLI group while liver injury preceded in DWOLI group (both $p<0.05$). Gastrointestinal

hemorrhage was more common in DWLI group ($p<0.05$) (table 2). The incidence of cough was 20.7% (44/213) in DWLI and 7.1% (27/379) in DWOLI group, respectively. while the incidence of breathlessness was 3.8% (8/213) and 0.5% (2/379), respectively. The difference were statistically significant respectively (χ^2=22.397, 6.724; p=0.000, 0.003). For subgroup analyses in DWLI group, the incidence of cough and breathlessness in SD subgroup were significantly higher than that in dengue group (χ^2=7.118, 9.148; p=0.008, 0.011, respectively). The involvement of other organs such as liver, kidney, heart, skeletal muscle were significantly higher in SD subgroup than dengue subgroup (all $p<0.05$). Meanwhile, MODS was more frequent in SD subgroup ($p<0.05$).

Laboratory findings

The results showed that the total leukocyte count, neutrophil count, lymphocyte count and platelet count of dengue patients were all decreased, among which the lymphocyte count of DWLI group was significantly lower than that of DWOLI group ($p<0.05$, table 3). Cholinesterase decreased slightly in both groups, with DWLI group statistically lower ($p<0.05$, table3). The difference of serum creatinine (Scr), myoglobin (MYO), prothrombin time (PT), C-reactive protein (CRP) and pro-calcitonin (PCT) were statistically significant, with DWLI higher for all parameters (all $p<0.05$, table 3). However, the lever of Aspartate transaminase (AST), Alanine aminotransferase (ALT) were not comparable between the two groups ($p>0.05$). For subgroup analyses in DWLI group, the value of AST, ALT, MYO, Creatine kinase (CK), Creatine kinase myocardial isoenzyme (CK-MB), Lactate dehydrogenase (LDH) were significantly higher in SD subgroup than those of dengue subgroup ($p<0.05$) (table 4).

Radiographic Findings

The chest images of 213 patients in DWLI included inflammatory exudation, increasing of lung markings, pleural effusion, pleural thickening and interstitial pneumonia. The ratios for the above radiographic findings were 60.1% (128/213), 39.4% (84/213), 8.5% (18/213), 6.6% (14/213), 0.5% (1/213), respectively. Further statistical analysis of subgroups showed that the incidence of pleural effusion in SD subgroup was higher than that in dengue subgroup (χ^2=9.502, p=0.001, table 5) (Figure 1). Thickening of lung texture in SD subgroup was statistically higher than that in dengue subgroup (χ^2=32.494, p=0.000, table 5). Pulmonary inflammatory exudation included bilateral one with 84 cases and unilateral one with 44 cases (Figure 2). The incidence of bilateral one in SD subgroup was statistically higher than that in dengue subgroup while unilateral one was more common in dengue subgroup (χ^2=5.003, p=0.025, table 6).

Treatment and prognosis

All cases were treated according to the diagnosis and treatment guidelines of dengue fever. Antitussive therapy and oxygen inhalation were given to those with cough and breathlessness. The antiviral ratios in DWLI and DWOLI groups were 38.0% (81/213), 24.8% (94/379) respectively, antibacterial treatment ratios were 36.2%(77/213), 7.7% (29/379), the combination therapy ratios were 15.5% (33/213), 2.6% (10/379),

all of whose differences were statistically significant (χ^2=11.456, 75.343, 33.451; all p<0.001; table 7). In DWLI group, of 18 patients with pleural effusion, 1 patient received closed drainage, 5 patient received diuretic therapy (furosemide), the rest were treated with conservative treatment, all pleural effusion subsided. There were 10 cases in DWLI group complicated with MODS, among which 7 cases received ventilator-assisted ventilation and 4 cases received continuous renal replacement therapy. The median length of stay in both groups was 5 days. 2 patient with MODS died and the other patients were cured. No recurrence was found during follow-up.

Discussion

The pathological basis of dengue fever is systemic inflammation caused by dengue virus infection. With the development of dengue virus and its serotype detection technology, it is found that some serotypes of dengue virus are easy to cause severe dengue and multiple organ function damage [10]. In the past, it was thought that the lung was not the most common organ affected by dengue fever. Instead, attention paid to lung involvement was mainly on severe cases with pulmonary hemorrhage [11]. However, lung is the most vulnerable organ of systemic inflammatory response. With the increasing incidence of dengue fever and the popularity of imaging examination in recent years, the incidence of pulmonary involvement in dengue fever has increased significantly [12, 13].

In this study, the proportion of patients with SD was as high as 35.8% (212/592). There are several reasons for the high proportion of SD in the study. Firstly, recent dengue virus serotype infection prevalent in Guangdong Province was easy to cause severe cases [14, 15]. Secondly, our hospital is the designated unit for the management of SD. Lastly, those asymptomatic or mild dengue may not come to hospital or just went to clinics for treatment. The study found that the ratio of SD in DWLI group was particularly higher than that in DWOLI group. The general data of this study showed that dengue fever patients who were old, smoking population, accompanied by underlying diseases such as hepatobiliary disease, hypertension, diabetes, coronary heart disease were prone to have lung involvement. It is known that dengue virus causes more SD in the elderly and those with underlying diseases than otherwise. Lung involvement is probably one of the early manifestations and pathological mechanisms.

The incidence of cough and breathlessness in DWLI group was significantly higher than that in DWOLI group. Further analysis showed that the above symptoms were mainly in SD subgroup, implying that cough and breathlessness can be used as the observation index of SD with lung involvement, there were no studies before reporting the great value of cough and breathlessness in identifying SD. The lymphocyte count in DWLI group was significantly lower than that in DWOLI group, the cholinesterase was also significantly lower while the myoglobin increased. The pathological mechanism may be the intense inflammatory reaction induced by the high viral load, which caused numerous damage to lymphocyte, liver cells and muscle cells. The increase of C-reactive protein (CRP) and pro-calcitonin (PCT) reflected the increase of inflammatory response in DWLI patients. Imaging examination showed that pleural effusion and bilateral pneumonic exudation were associated with SD. Therefore, in areas with

pandemic dengue fever, it is necessary to consider that lung involvement in dengue fever is one of the causes of pneumonia, and for these patients should be warned of SD.

In-depth study on the pathogenesis of dengue virus showed that in the early stage of virus infection, the organ-specific (Brain, lung, retina) tight junction of microvascular endothelial cells was destroyed, which would increase exudation [16]. NS1 was thought to be the intriguer [17]. Other study found that plasma leakage was caused by the decrease of plasma concentration of sphingosine-1-phosphate, which protected endothelial cell [18]. Since the lung is the organ most vulnerable to exudation and edema in inflammatory reaction, these mechanisms explained why clinical symptoms such as cough, breathlessness, pleural effusion emerged more often in DWLI patients. The advanced mechanism of lung involvement is mainly focused on endothelial cells and peripheral organs. High mobility group protein 1 (HMGB1) is an important regulator of inflammatory response. It was highly activated in the lungs and peripheral organs in patients died of dengue [19]. Lung and peripheral organ damage due to inflammatory reaction contributed to the same pathological mechanism of lung involvement and SD. Therefore, once lung involvement is present, more attention should be paid to the risk of SD or even MODS. In this study, it was found that there was a clear correlation between bilateral pneumonic exudation and SD. It was also found that patients with lung involvement were prone to acute liver, kidney damage and MODS.

In addition, the relationship between lung involvement and severity of dengue fever relies on two aspects, the pathogenicity of the virus itself and other complicated infections. Firstly, the high viral load or reinfection patients in the course of the disease can cause serious lung and multiple organ functional damage [20, 21]. Micro abscesses existed in heart, brain, lung and kidney of the reported dengue cases with MODS after autopsy [5]. Secondly, other complicated infections such as *staphylococcus aureus*, fungi or influenza A virus could aggravate the lung damage or even induce pulmonary cavity, acute respiratory distress syndrome (ARDS) and MODS [22–25]. Therefore, patients with lung involvement need more surveillance on their risk of more advanced disease. Active measures include timely discover of ARDS caused by dengue fever, early utilization of noninvasive mechanical ventilation [26, 27], timely cardiac ultrasound examination for dengue fever patients with respiratory distress, and monitoring of systemic hemodynamics such as cardiac output and blood volume [28, 29].

Most dengue fever patients with lung involvement can be relieved after active treatment. However, there are reports showing patients with large volume pleural effusions needed emergent puncture and drainage. There are also reports of acute lung injury after platelet transfusion of ordinary dengue patients, which indicates that the treatment of dengue fever patients with lung involvement should be active and cautious [30]. In this study, the proportion of anti-virus, anti-bacteria and the combination therapy in DWLI group were significantly higher than that in DWOLI group. Combined with the analysis of the increase of CRP and PCT in DWLI group, the results implied that these patients had more serious inflammatory reaction and higher incidence of secondary bacterial infection. The prognosis of patients with lung involvement was worse than those without lung involvement. In this study, 10 patients complicated with MODS were all in DWLI group, and 2 of them died. At present, there are few studies exploring how to

prevent lung damage and progression to SD. The above mentioned NS1 may be one of the effective targets for prevention and treatment.

Though the present study gave some insight to the understanding of SD, it still had some limitations. Firstly, it was a single-center retrospective study, it may had selective bias since different types of patients may go to different hospitals for therapy. Secondly, it lacked the analyses of the influence of serotypes on the outcome of patients since many patients didn't have it tested. Lastly, not all patients undergone CT scan due to the cost and radioactivity, and sensitivity of X-ray is much lower. Therefore, a more well-designed, multicenter, serotype involved prospective study is expected to demonstrate the value of lung involvement in dengue management.

Conclusion

In conclusion, among dengue fever patients, the elderly, smoking population, those accompanied by underlying diseases including hepatobiliary disease, hypertension, diabetes, coronary heart disease were prone to have lung involvement. The proportions of clinical manifestations such as cough, breathlessness, pleural effusion and bilateral pneumonic exudation were increased in SD patients. Bilateral pneumonic exudation in particular was a sign of SD. Thus in clinical practice, we should be aware of lung involvement in all dengue patients. For those who had apparent lung injury such as cough, breathlessness, pleural effusion and pneumonic exudation, we should maintain sharp vigilance on whether they were SD or progressing to SD so that to take timely and proper measures to manage them and improve their prognosis.

Abbreviations

ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate transaminase; CHE: cholinesterase; CHD: coronary heart disease; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; CNS: central nervous system; CRP: C-reactive protein; CT: computerized tomography; CVD: cerebro vascular disease; DM: diabetes mellitus; DT: digestive tract; DWLI: dengue with lung involvement; DWOLI: dengue without lung involvement; Fib: fibrinogen; HD: hepatic and gall diseases; HP: hypertension; INR: international normalized ratio; IRB: Institutional Review Board; LDH: lactic dehydrogenase; LYMPH: lymphocyte; MODS: Multiple organ dysfunction syndrome; MS: Musculoskeletal system; MYO: myoglobin; NEUT: neutrophil; NS1 Non-structural protein 1; PCR: Polymerase chain reaction; PCT Pro-calcitonin; PLT: platelets; PT: prothrombin time; PTA: Prothrombin activity; Scr: serum creatinine; SD: severe dengue; WBC: white blood cell.

Declarations

Ethics approval and consent to participate

This study obtained ethical approval from the Institutional Review Board (IRB) of the Third Affiliated Hospital of Sun Yat-Sen University ([2019]02-459-01). All patients provided written informed consent to use their clinical data.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Yunfeng Shi and Weiqiang Gan conducted the main study and wrote the manuscript; Xiaohan Shi and Jingjing Liang collected the data and did the analyses; Xiaoxia Chen helped to search the diagnosis in the database and provided the name list of the patients; Yuefei Guo read the imagings of all patients; Yuwei Tong helped to monitor the quality of the study; Zhiliang Gao and Benquan Wu developed the study idea and supervised Yunfeng Shi and Weiqiang Gan.

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Tables

Table 1 Underlying disease between dengue with and without lung involvement *n*(%)

Groups	HD	HP	DM	CHD	CVD
DWLI(n=213)	60(28.2)	48(22.5)	20(9.4)	17(8.0)	15(7.0)
DWOLI(n=379)	75(19.8)	28(7.4)	7(1.8)	14(3.7)	8(2.1)
χ^2	5.440	27.961	18.840	5.051	8.881
P	0.020	0.000	0.000	0.025	0.003

Hepatic and gall diseases include chronic cholecystitis, hepatolithiasis and chronic viral hepatitis. DWLI: dengue with lung involvement; DWOLI: dengue without lung involvement; HD: hepatic and gall diseases; HP: hypertension; DM: diabetes mellitus; CHD: coronary heart disease; CVD: cerebro vascular disease

Table 2 Organ injury between dengue with and without lung involvement *n*(%)

Groups	Blood	MS	Liver	Kidney	Heart	DT	CNS	MODS
DWLI(*n*=213)	103(48.4)	83(39.0)	67(31.5)	16(7.5)	19(8.9)	8(3.8)	2(0.9)	10(4.7)
DWOLI(*n*=379)	188(49.6)	144(38.0)	170(44.9)	4(1.1)	28(7.4)	4(1.1)	2(0.5)	0(0)
χ^2	0.085	1.859	10.199	15.492	0.414	3.740	0.004	20.751
P	0.771	0.395	0.001	0.000	0.520	0.053	0.949	0.000

MS: Musculoskeletal system; DT: digestive tract; CNS: central nervous system; MODS: multiple organ dysfunction syndrome

Table 3 Laboratory findings between dengue with and without lung involvement

Blood test items	Test value(median value)		*Z*	*P*
	DWLI	DWOLI		
WBC ($\times10^9$/L)	2.73(1.96~4.69)	2.83(2.07~4.25)	-0.147	0.883
NEUT($\times10^9$/L)	0.61(0.49~0.72)	0.55(0.39~0.68)	-3.696	<0.001
LYMPH($\times10^9$/L)	0.27(0.16~0.36)	0.32(0.20~0.44)	3.756	<0.001
PLT($\times10^9$/L)	76.0(48.0~131.0)	80.0(49.0~128.0)	0.532	0.595
AST(U/L)	65.0(36.3~97.3)	55.5(33.0~89.0)	-1.423	0.155
ALT(U/L)	40.0(25.0~62.8)	34.0(21.0~60)	-1.602	0.109
ALP(U/L)	54.0(44.0~65.0)	50(39.0~63.0)	-2.264	0.024
CHE/(U/L)	6307(5510~7503)	6878(5957~8113)	2.786	0.005
Scr(μmol/L)	76.0(63.5~93.0)	71.0(57.0~84.0)	-3.168	0.002
MYO/(μg/L)	42.6(27.8~101.0)	35.4(17.1~65.4)	-2.860	0.004
PT /s	13.2(12.5~13.9)	12.9(12.5~13.6)	-3.458	0.001
PTA (%)	102.0(88.0~112.0)	104.0(94.0~113.0)	2.902	0.004
Fib /(g/L)	2.93(2.51~3.31)	2.80(2.51~3.10)	-2.849	0.004
INR	0.99(0.93~1.08)	0.97(0.93~1.04)	-3.230	0.001
CRP/(mg/L)	6.35(2.18~20.65)	4.00(1.90~9.50)	-2.836	0.005
PCT/(ng/L)	0.23(0.15~0.39)	0.15(0.10~0.26)	-4.017	0.000

WBC: white blood cell; NEUT: neutrophil; LYMPH: lymphocyte; PLT: platelets; ALP: alkaline phosphatase; CHE: cholinesterase;Scr: serum creatinine; MYO: myoglobin; PT: prothrombin time; PTA: Prothrombin activity; Fib: fibrinogen; INR: international normalized ratio; CRP: C-reactive protein; PCT: procalcitonin.

Table 4 Laboratory findings between SD subgroup and dengue subgroup in lung involvement group

Blood test items	Test value(median value)		*Z*	*P*
	SD	dengue		
AST(U/L)	78.0(51.8~135.5)	55.0(37.0~86.0)	-2.415	0.016
ALT(U/L)	45.0(32.0~85.3)	35.0(24.0~57.0)	-2.496	0.013
CK(U/L)	264.5(159.0~579.0)	139.0(85.0~226.0)	-3.653	0.000
CK-MB(U/L)	11.0(7.8~16.8)	8.0(6.0~10.0)	-3.134	0.002
LDH(U/L)	328.0(244.0~491.8)	268.0(227.0~326.0)	-2.302	0.021
MYO/(μg/L)	88.2 (33.9~137.6)	38.04(22.6~59.9)	-4.473	0.000

ALT: alanine aminotransferase; AST: aspartate transaminase; CK: creatine kinase ; CK-MB: creatine kinase isoenzyme ; LDH: lactic dehydrogenase; MYO: myoglobin.

Table 5 Imageology between SD subgroup and dengue subgroup in lung involvement group *n*(%)

Subgroups	Inflammatory exudation	Increase of lung markings	Pleural effusion	Pleural thickening
SD(*n*=122)	99(82.8)	28(23.0)	17(13.9)	8(6.6)
dengue(*n*=91)	29(31.9)	56 (61.5)	1(1.1)	6(6.6)
χ^2	57.782	32.494	9.502	0.000
P	0.000	0.000	0.001	0.992

SD: sever dengue

Table 6 Infiltration change of imageology between SD subgroup and dengue subgroup in involvement group *n*(%)

Subgroups	Bilateral inflammatory exudation	Unilateral inflammatory exudation
SD(*n*=99)	70(70.7)	29(29.3)
dengue(*n*=29)	14(48.3)	15(51.7)
χ^2	5.003	
P	0.025	

SD: sever dengue

Table 7 Antiviral / antibacterial treatment between dengue with and without lung involvement *n*(%)

Groups	Antiviral treatment	Antibacterial treatment	Both antiviral and antibacterial treatment
DWLI(n=213)	81(38.0)	77(36.2)	33(15.5)
DWOLI(n=379)	94(24.8)	29(7.7)	10(2.6)
χ^2	11.456	75.343	33.451
P	0.001	0.000	0.000

DWLI: dengue with lung involvement; DWOLI: dengue without lung involvement

Figures

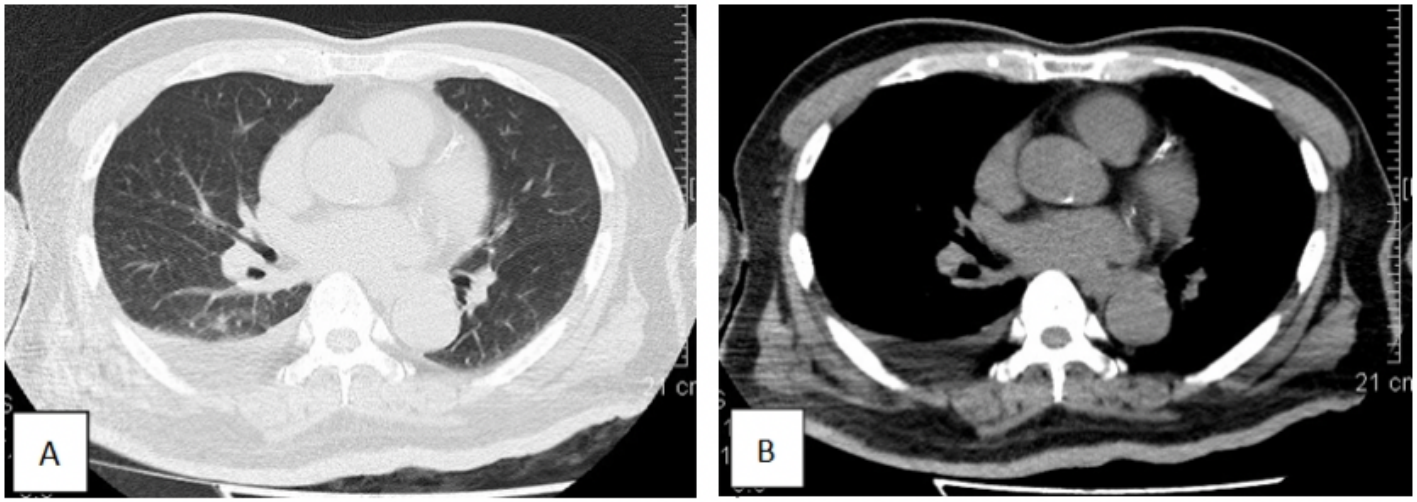

Figure 1

Chest CT scan of case with inflammatory exudation and pleural effusion. Axial CT images-A lung window setting, and B mediastinal window showed mild bilateral inflammatory exudation and right pleural effusion.

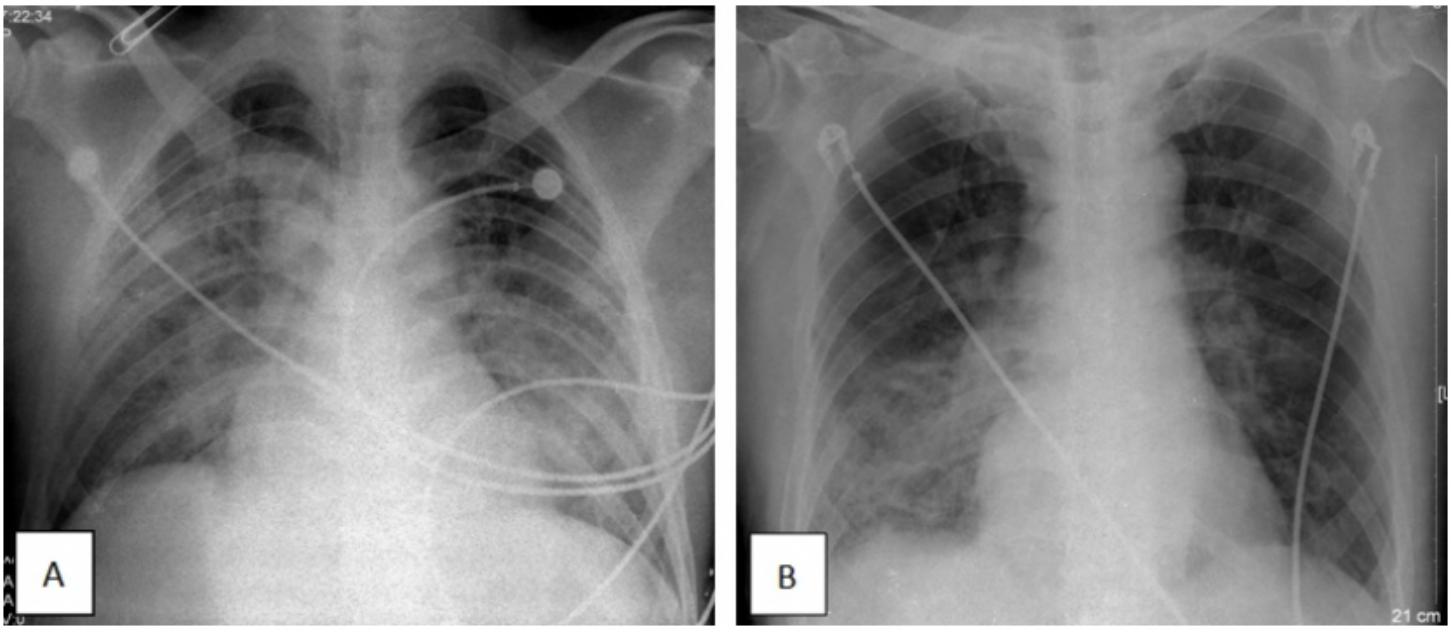

Figure 2

Chest X-ray of cases with inflammatory exudation. Picture A showed bilateral inflammatory exudation. Picture B showed unilateral inflammatory exudation, which mainly located at right lower lung.