Clinical and Laboratory Features of Dengue Fever Patients in Riau, Indonesia

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Abstract

Background

Dengue fever is one of the most important viral diseases, especially in the tropics. According to WHO, nearly 50 million people are infected with dengue each year, and WHO estimates that almost half of the world's population lives in countries where dengue is endemic. This study aims to determine the clinical and experimental characteristics of patients with dengue fever in order to better understand the disease.

Method

From December 2021 to January 2022, a cross-sectional study of fever patients was conducted on Kerumutan Public Health Center and Selasih District General Hospital, Riau, Indonesia. Blood samples were collected from suspected cases of dengue and tested against dengue-specific IgM antibodies by enzyme-linked immunosorbent assay (ELISA). Research participants who met the selection criteria were included in the study. Laboratory findings were recorded and hematological and biochemical parameter tests were performed.

Result

A total of 50 cases of dengue fever were included in the study during the study period. Of these, 8 (16%) were children and 42 (84%) were adults between the ages of 1 and 76. The most common clinical symptoms were fever (100%), headache 41 (82%), myalgia 42 (84%), and nausea / vomiting 38 (76%). Cohematological findings were thrombocytopenia 28 (56%), followed by anemia 22 (44%) and leukopenia 15 (30%), with elevated biochemical parameters of AST 24 (48%) and ALT 8 (16%).

Conclusion

This study highlights the most common clinical and laboratory profiles for dengue virus infection. This may warn doctors of possible dengue virus infections in the study area.

Keyword : Dengue Fever, Clinical Feature, Laboratory Feature

Introduction

Dengue is a mosquito-borne arboviral disease that poses a major global public health threat that is widespread in the tropical and subtropical regions of the world, primarily urban and suburban areas [1]. WHO estimates that more than 2.5 billion people are at risk of dengue infection in more than 100 countries, and about 510 million people are infected with dengue fever each year [2]. Of these, 500,000 cases of severe dengue are diagnosed each year and 24,000 die annually [3,4,5,6]. Dengue is endemic in the WHO region of Africa, the Americas, the Eastern Mediterranean, Southeast Asia, the Western Pacific, and the Caribbean [7].

Over the last few decades, the global incidence of dengue virus (DENV) infection has increased with increasing geographic expansion into new countries [8]. The threat of possible dengue outbreaks was first reported in 2013 in Dire Dawa, Ethiopia. In this outbreak, 11,409 suspected cases of dengue fever were reported in 4 months. Fifty (50/88; 56.8%) specimens were reported positive for dengue infection, with the most affected age group being 1544 years [9]. In late 2014, cases of dengue fever were also reported from the Somali region of Ethiopia, and 33 (33/57, 57.9%) samples were reported to be positive for dengue fever [10]. The main causes of the widespread and increasing incidence of dengue fever are unplanned rapid urbanization and migration to urban areas, poor hygiene that contributes to fertilization of mosquito breeding grounds, and control of mediators. Lack of climate change [11].

Mosquitoes are widespread in Africa and can act as carriers of the dengue virus, increasing the risk of epidemics in African countries, coupled with rapid population growth, unplanned urbanization and increased travel abroad. There is sex [12]. There is no specific cure for dengue fever, but early detection and fluid replacement therapy, as well as careful use of analgesics and antipyretics, significantly reduce severe case mortality from 20% to less than 1% [13]. In clinical practice, patient diagnosis and treatment is known to be based on clinical symptoms and abnormal laboratory findings [14]. The first DENV infection can be asymptomatic [15] or lead to non-

specific febrile illness. It is usually accompanied by sudden fever, severe headache, bone, joint and muscle pain, mild bleeding, weakness, myalgia, and skin rash [16]. All of these clinical symptoms are similar to many other febrile illnesses that are prevalent in the country. Malaria, Kala Azar, typhoid fever, etc., which pose a diagnostic problem for dengue fever [17].

Dengue fever is caused by infection with one of four serotypes of DENV, a single-stranded arbovirus RNA virus of the genus Flavivirus [18]. Infection with a dengue serotype provides lifelong isomorphic immunity to that particular serotype. Due to the circulation of different serotypes during an epidemic, it is possible to eventually infect each serotype once, up to four times [19]. Subsequent infections with different DENV serotypes have been well documented to increase the risk of developing severe dengue [20, 21]. Dengue infection can be diagnosed based on clinical symptoms and laboratory tests. Among clinical tests, non-specific tests; hematological parameters, liver function tests, serum protein concentration, specific tests, etc. Antibodies can be detected using viral antigen testing, genomic sequencing, serology, and more [22, 23].

Physicians need to be aware of the most common clinical and hematological and biochemical symptoms that are important in the clinical management of a patient and therefore important for saving lives. Therefore, this study aimed to highlight the most common clinical features, hematological and biochemical findings of dengue cases.

Methods

Study area and participants

A cross-sectional prospective, hospital-based study was carried out in Kerumutan Public Health Center and Selasih District General Hospital, Riau, Indonesia from December 2021 to January 2022.

Inclusion criteria

Febrile patients who were presumed for dengue infection based on 2009 WHO criteria [8] and serologically confirmed with dengue specific IgM antibody. The febrile patient is referred to one whose axillary temperature is ≥ 38 oC.

Exclusion criteria

Cases confirmed as malaria, typhoid fever, and any other confirmed chronic diseases were excluded in the study.

Data collection

Laboratory tests were performed by doctors for each study participant. Demographic variables and clinical profiles of study participants published in a previous study [24] were collected from nurses using a structured questionnaire. Diagnosis of dengue fever was based on a positive enzyme-linked immunosorbent assay (ELISA; EUROIMMUN Diagnostics) [25] for specific IgM antibodies against dengue fever in serum. All routine investigations such as hematological measurements such as total white blood cell count (TLC), differential white blood cell count, and platelet count. Hemoglobin (Hgb) and hematocrit (Hct) were measured using an automated blood analyzer (CELLDYN 1800, Abbott Laboratories Diagnostics Division, USA). Thick and thin blood smear of malaria parasite, biochemical test; AST and ALT for liver function test, creatinine and BUN for renal function test, total protein using automatic biochemical analyzer (Vegasys) I did [26]. The cutoff

value for each test result was considered based on the reference range used in the lab. In addition, medical records of all dengue-specific IgM-positive cases were reviewed to collect further information (eg, typhoid fever and all other confirmed chronic cases).

Statistical analysis

Data were entered and analyzed using the SPSS 20.0 statistical software. Descriptive statistic was used to calculate frequency and percentage. Data were presented by using tables and figure.

Results

Clinical profiles of dengue cases during a hospital visit

During the study period, 50 50 patients are willing to be recruited as the study sample. thirty-eight (76%) study participants were males. A study participants' age varied from 1 year to 76 years. forty-two (84%) study participants were ≥ 15 years (Table 1).

Table 1. Gender and age of study participants (N = 50)

Variables	Number of participants (N)	Percentage (%)
Gender		
Male	38	76
Female	12	24
Age < 15 years	8	16
≥ 15 years	42	84

The commonest clinical feature was fever, 50 (100%), followed by headache in 41 (82%), myalgia 42 (84%), nausea/vomiting 38 (76%), abdominal pain 29 (68%), eye pain and mucosal bleeding 23 (46%) and 33 (66%) in each of the cases. Rashes and tourniquet test in 12 (24%) and 26 (52%) of cases were seen, respectively. conjunctival hemorrhage and hepatomegaly 8 (16%) and 9 (18%)in each of the cases. (Table 2).

Table 2. Clinical features of dengue fever patients at the time of admission to the hospital (N=50)

Clinical feature	Number of cases	Percentage
Fever	50	100
Abdominal distention	10	20
Headache	41	82
Eye pain	23	46
Myalgia	42	84
Mucosal bleeding	33	66
Abdominal pain	29	58
Nausea and vomiting	38	76
Rash	12	24
Tourniquet test	26	52
Conjunctival hemorrhage	8	16
Hepatomegaly	9	18

Hematological profiles of dengue cases during a hospital visit

The most common hematological finding observed was thrombocytopenia (platelet count <140,000/μL) in 28 (56%), followed by anemia (hemoglobin level < 11.5 g/dl) in 22 (44%)

and leucopenia (total leukocyte count < 4,000/µL) in 15 (30%) of the cases. Hematocrit > 44% were noted in 5 (10%) of the cases. Neutrophil < 1500 in 1 (34%) and lymphocyte > 2900 in 19 (18%) of the cases were noticed (Table 3).

Table 3. Hematological parameters of dengue cases at the time of hospital visit (N = 50)

Hematological test	No. of patient (N)	Percentage (%)	Normal lab value
Platelet count (cells/µL)			140,000-415,000/µL
< 140,000	28	56	
≥140,000	22	44	
WBC count (cells/µL)			4,000-10,500/µL
< 4,000	15	30	
≥ 4,000	35	70	
Hemoglobin g/dl			
Male ≤ 13	10	20	M: 13-16
Female ≤ 12	12	24	F: 12-15
Sub-total	22	44	
Hematocrit (%)			
Male > 46	3	6	M: 38-46
Female > 44	2	4	F: 35-44
Sub-total	5	10	
Neutrophil (cells/µL)			1500-8000
< 1500	17	34	
≥ 1500	33	66	
Lymphocyte (cells/µL)			900-2900
≤ 2900	41	82	
> 2900	9	18	

Biochemical parameters of dengue cases at the time of hospital visit

The results of the biochemical investigation revealed that alanine aminotransferase (ALT) level > 42 IU/L was observed in 8 (16%) of cases and aspartate aminotransferase (AST) level > 37 IU/L observed in 24 (48%) of cases. Creatinine level > 1.1 mg/dl was observed in 10 (20%) and BUN > 23.5 mg/dl noted in 12 (24%) of cases. Hypoproteinaemia (total protein value < 6.6 mg/dl) was observed in 11 (22%) cases (Table 4).

Table 4.Biochemical parameters among dengue cases (N = 50)

Parameter	No. of cases (N)	Percentage (%)	Normal lab value
ALT (IU/L)			3-42 IU/L
≤ 42	42	84	
> 42	8	16	
AST (IU/L)			5-37 IU/L
≤ 37	26	52	
> 37	24	48	
Creatinine (mg/dl)			0.6-1.1 mg/dl
≤ 1.1	40	80	
> 1.1	10	20	
BUN (mg/dl)			4.7-23.5 mg/dl
≤ 23.5	38	76	
> 23.5	12	24	
Total protein (mg/dl)			6.6-8.7mg/dl
< 6.6	11	22	

≥ 6.6	39	78

Discussion

Over the last few decades, the global epidemic of dengue has increased dramatically due to the limitations of currently available management strategies such as vaccines and pesticides [27, 28]. Therefore, early diagnosis and appropriate treatment are of utmost importance. Because dengue is a recently recognized problem in Ethiopia [9, 10], knowledge of clinical symptoms and laboratory tests for dengue is essential for patient management. Therefore, the focus of this study was to document the first baseline data on clinical symptoms, hematological and biochemical parameters of patients with dengue fever in the country. The evidence generated is essential for the proper treatment of patients with dengue fever.

In this study, consistent with other studies, the most common clinical symptoms were fever, followed by headache, muscle pain, nausea / vomiting, and abdominal pain [29, 30]. In our study, rash was observed in 12.7% and hepatomegaly in 22.5%, but in another similar study, rash and hepatomegaly were found in 28.1% and 12.5% of patients, respectively. It was [31]. Bleeding diathesis is a common clinical manifestation of dengue fever due to decreased platelet count and leakage from blood vessels. This is due to the stimulation of immunological mechanisms by which the interaction of the dengue fever virus with host cells causes the release of excessive cytokines, leading to changes in the vascular endothelium, mononuclear cell infiltration, and perivascular edema [32]. Mucosal bleeding was observed in most patients in our study, consistent with other studies [33], but in contrast to another study [34], which showed skin bleeding as the most common bleeding symptom. am. Another study reported bleeding symptoms only in the form of petechiae [31]. Differences in clinical symptoms from different studies can be attributed to differences in virus strains and their virulence factors.

Among the hematological profiles, thrombocytopenia is the most common finding in this study, which is consistent with other studies [35, 36]. Thrombocytopenia may be due to decreased platelet production due to bone marrow virus suppression, and increased binding of dengue antigens to platelets and increased antibody-mediated platelet immunological destruction [37,38]. Leukopenia is one of the hematological parameters that occur in people affected by myelosuppression of dengue fever [38]. In our study, leukopenia was observed in 26.5% of cases, while in other studies leukopenia was observed in 56.9% [39] and 50% of cases [40].

Hemoglobin levels below the cutoff level were observed in 45 patients (44.1%). This may be due to mucosal bleeding, with 38 (37.3%) showing bleeding. This finding is consistent with another study [41]. In our study, an increase in hematocrit was observed in 6.9% of cases, which is higher than in other studies reported an increase in hematocrit of 50% [42] and 27% [40]. It is low. This may be associated with increased severity and is explained by blood levels due to increased plasma blood permeability, which is a fundamental pathophysiological change in dengue fever.

In this study, higher than normal levels of AST were observed in 45.1% of cases, ALT was observed in 17.6% of cases, and more cases than ALT showed elevated AST levels. This is consistent with other studies that reported higher AST and ALT levels in 68.5% and 39.2% of cases, respectively [43], with similar results increased in 72.7% of AST and ALT levels. In 27.3% of cases reported at the location of [43]. 44]. The dengue virus is hepatotrophic and damages other organs. Therefore, the observed pattern can be explained by the over-release of AST from muscle cells (non-liver sources) damaged during infection, resulting in greater AST damage than ALT. ALT is primarily associated with hepatocytes and has the lowest activity in the heart and skeletal muscle, and AST is found in red blood cells, kidney and brain tissue, heart and skeletal muscle, usually with damage to these sources and the liver. Elevated due to response to damage [45].

Serum creatinine and blood urea (BUN) levels were elevated in 19.6% and 14.7% cases, respectively. These may result from direct viral effects on glomeruli and tubular cells, or tissue damage caused by a deregulated host immune response to viral antigens [46]. Hypoproteinemia was observed in 21.6% of cases. It is possible that viruses, host immune responses, and complex interactions between endothelial cells impair the integrity and function of the vascular endothelial cell barrier, causing plasma leakage and causing hypoproteinemia [47].

These are some limitations of research. Due to the nature of the cross-sectional study design, these cases of dengue were not compared to controls and continuous hematological and biochemical changes. These may be done in the future to better understand the symptoms of dengue virus infection.

Conclusion

The most important guides for the treatment and prognosis of dengue fever are recognition of clinical features and laboratory findings such as hematological and biochemical parameters. In this study, the most common complaint in patients with dengue was fever, followed by headache and myalgia. The most common findings identified were thrombocytopenia, anemia, leukopenia, and elevated AST levels. Therefore, these findings should warn physicians about the potential for dengue infection in the study area.

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