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Original Article

Age and Gender-Based Clinical and Laboratory Features in Dengue Infection: A Comparative Study

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Abstract

Background: Dengue infection remains prevalent globally, with a shift toward adult cases. WHO diagnosis relies on clinical and laboratory criteria to identify and manage the disease effectively.

Aim: This study aims to investigate the differences in clinical and laboratory findings of dengue infection based on age and gender.

Materials and methods: This analytical cross-sectional study utilized medical record data from 162 pediatric and adult dengue patients diagnosed with dengue fever (DF) or dengue hemorrhagic fever (DHF) in Surabaya hospital in 2022. The study assessed hemoglobin, hematocrit, leukocyte, and platelet levels across six age groups: toddlers (0–5 years), children (6–10 years), adolescents (11–18 years), young adults (19–29 years), and adults (30–59 years). The variables observed in this study include age, gender, classification, and type of dengue infection among hospitalized patients diagnosed with dengue.

Results: The findings of this study indicate no statistically significant difference between pediatric and adult patients regarding the classification of DF and DHF ($p = 0.085$). However, laboratory results revealed a significant difference in the incidence of thrombocytopenia between children and adults ($p = 0.019$). Furthermore, a significant association was found between platelet count and dengue classification, with lower platelet levels observed in DHF cases compared to DF ($p = 0.001$).

Conclusions: This study shows significant clinical and laboratory differences between children and adults with dengue, highlighting the necessity of age-specific diagnostics to enhance early detection and appropriate treatment.

Key words: adults; children; dengue; human; health; medicine.

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Introduction

Dengue virus infection is a serious worldwide health issue that is mostly seen in tropical and subtropical regions. It is caused by one of four antigenically unique serotypes (DENV1 to DENV4). *Aedes aegypti* and *Aedes albopictus* are the main vectors of dengue infection, which can cause a wide range of clinical manifestations, from asymptomatic cases and mild dengue symptoms to severe symptoms like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [1,2].

Dengue prevalence significantly increased globally over the past two decades, from 500,000 cases in 2000 to over 5.2 million in 2019, according to the World Health Organization (WHO) [3]. Additional spikes were expected in 2024, with over 7.6 million cases and more than 3,000 deaths linked to the disease by April of that year [4]. Southeast Asia, in particular, remained a hyperendemic region with intense and year-round dengue transmission.

In Indonesia, dengue continues to pose a serious public health challenge. The incidence rate of DHF has fluctuated between 24.8 and 78.9 cases per 100,000 population from 2013 to 2023. As of June 2024 (week 22), Indonesia has reported 119,709 dengue cases and 777 deaths [4]. As a result, surveillance systems and WHO guidelines have been put in place to standardize clinical management and control efforts, and dengue has been elevated to a national health concern.

In hyperendemic regions, children under the age of 15 are more likely to develop dengue hemorrhagic fever (DHF), which is linked to recurrent dengue infections. On the other hand, DHF is becoming more common among adults. The abrupt development of a high fever is the indicator of DHF, which shares early febrile phase signs and symptoms with Dengue Fever (DF). Common hemorrhagic diseases include petechiae, easy bruising, positive tourniquet test (TT), and, in extreme situations,

gastrointestinal bleeding. Due to plasma leakage, hypovolemic shock (dengue shock syndrome) might occur toward the conclusion of the febrile period [5]. Age, comorbidities, immune status (primary vs. secondary infection), and socioeconomic circumstances are some of the risk factors that contribute to the development of severe dengue [6-8].

The understanding of dengue infection's age group and clinical severity is limited, possibly due to increased adult patient reports, differences in serological coverage in different endemic areas, or variations in dengue virus strain virulence [9]. Adults and children exhibit very different clinical manifestations. Classic dengue symptoms like a high fever, headaches (particularly retro-orbital ones), myalgia, and arthralgia are frequently reported by adults. On the other hand, children are more likely to experience rapid progression to Dengue Shock Syndrome (DSS) and plasma leakage and often present with nonspecific symptoms such as diarrhea, rash, and vomiting [1,8]. As an example, a study by Florez *et al.* has shown that adults are more likely to have back pain, hematuria, elevated hematocrit (HCT), and basophilia, while children under the age of 12 are more likely to have hypotension, lymphocytosis, and thrombocytopenia [8].

In Indonesia, a study observing dengue cases from hospitals in North Jakarta has shown that leukopenia and thrombocytopenia are significantly more common in dengue-positive patients [4]. Excessive platelet breakdown during a dengue infection, followed by leakage or bleeding, is a common cause of thrombocytopenia in dengue patients [10,11]. Probable dengue infection is defined as the presence of a low white blood cell count (< 4,000) and a low thrombocyte count (< 100,00) or hematocrit levels < 30% or > 55% [12]. Thrombocytes drastically decrease in severe dengue, but hematocrit and hemoglobin (Hb) increase as a result of plasma leakage. A higher hematocrit indicates plasma leakage in dengue, whereas a lower hematocrit indicates hemorrhage. Hematocrit monitoring is therefore essential for directing medical professionals in the appropriate management of dengue patients [13].

Infant-specific data from a tertiary hospital in East Java has revealed high rates of DHF among children under one year, with complications such as pleural effusion (66%), hypoalbuminemia (62%), hyponatremia (51%), and liver involvement (49%) [1]. Since prioritizing the management of severe dengue can lower morbidity and mortality, identifying risk factors helps achieve optimal care, prioritize resources for those at high risk of severe disease, and improve expert understanding of disease dynamics [12]. While risk identification in adults is focused on bleeding and organ dysfunction, among children, the primary focus is on early detection of issues like plasma leakage and hypovolemia [7,8]. Understanding the distinct clinical and laboratory features of the various dengue infection severities facilitates the development of effective management strategies and improved decision-making.

Materials and methods

This study was an analytical cross-sectional type, located in Surabaya, the Indonesian capital of the East Java province. With an area of over 333,063 km^2 and a population of about 3 million, Surabaya is the second-biggest city in Indonesia. The study was carried out at the tertiary teaching hospital, Universitas Airlangga Hospital, in Surabaya, Indonesia. The hospital serves as a referral center in addition to providing complete medical services, including infectious disease management, to both adult and pediatric patients.

This study utilized hospital medical records from 2022. All patients were diagnosed with dengue infection according to the 2011 WHO Dengue Guidelines. According to the WHO, dengue fever (DF) commonly affects older children, adolescents, and adults, presenting as an acute febrile illness (above 38 °C) that may be biphasic and accompanied by headache, myalgia, arthralgia, rash, leukopenia, and thrombocytopenia. Dengue haemorrhagic fever (DHF), on the other hand typically associated with secondary dengue infections. Characteristic clinical features include a positive tourniquet test (TT), petechiae, easy bruising, or gastrointestinal bleeding, along with consistent findings of thrombocytopenia and hemoconcentration before shock onset [14].

A total of 162 respondents, consisting of both pediatric and adult patients, were included in the study. Participants were categorized into five age groups: toddlers (0–5 years), children (6–10 years), adolescents (11–18 years), young adults (19–29 years), and adults (30–59 years). In this article, we have chosen to use the terms children and adults. Due to the limited number of patients, which should not significantly impact the pooled outcome, children were classified as those between the ages of toddlers and adolescents, and adults were defined as those between the ages of young adults and adults. The inclusion criteria were as follows: patients suspected of having dengue infection, falling within the specified age categories, showing clinical symptoms of dengue (specifically leukopenia, thrombocytopenia, elevated hemoglobin and

hematocrit levels), and not suffering from any severe comorbid infections. The exclusion criterion was: the patients had another infection other than dengue, or if the patient died during the treatment period in the hospital.

The laboratory data used in this study included the lowest values of leukocyte and platelet count, as well as the highest values of hemoglobin count and hematocrit. We specified leukopenia (≤ 5,000 mm^3/cell), thrombocytopenia (≤ 100,000 mm^3/cell), the highest value of hemoglobin, and hematocrit levels. In addition to observing common clinical symptoms of dengue such as fever, pain, and petechiae, these variables were selected because they align with the WHO criteria for DF/DHF and represent routine laboratory tests conducted in Indonesian hospitals for suspected dengue cases. It is important to note that Indonesia, as a middle-income and dengue-endemic country, rarely performs molecular examinations due to their high cost and limited availability of advanced laboratory facilities. The Sysmex XN-500 automated hematology analyzer was used to examine all hematological parameters.

The study has received ethical approval from the Ethics Committee of the Faculty of Medicine, Universitas Airlangga (Certificate No. 105/KEP/2022). Laboratory data were collected from patients' medical records at the hospital. All data were processed and analyzed using SPSS version 22.0. Descriptive statistics were used to present sample characteristics. Bivariate analysis was conducted using the Chi-square test, Mann-Whitney, and Kruskal-Wallis test to identify factors associated with dengue infection severity.

Table 1. Distributing of dengue fever patients in Universitas Airlangga Hospital during 2022.

Variable	n	%
Age category		
Toddler (0-5 years)	8	4.9
Children (6-10 years)	25	15.4
Adolescents (11-18 years)	42	25.9
Young adults (19-29 years)	47	29
Adults (30-59 years)	40	24.7
Gender		
Male	95	58.6
Female	67	41.4
Diagnosis		
DF	88	54.3
DHF	74	45.7

Results

In this study, we examined potential age-related variations in disease presentation by comparing and analyzing the hematological parameters of adults and children infected with dengue.

Table 1 shows the characteristics of Dengue patients who came to the hospital. The highest number of hospitalized dengue infection cases occurred among adolescents and young adults (25.9%). Based on the clinical symptoms, males were more frequently affected by dengue than females (58.6%). Furthermore, the diagnostic data indicate that cases of DF were more prevalent than those of DHF (54.3%).

Table 2 shows the comparison of age groups based on gender and the distribution of DF and DHF. Based on the chi-square analysis, no statistically significant differences were found ($p = 0.085$) in the DF and DHF groups among the age groups, although the highest

Table 2. Symptoms and diagnostic characteristics by age category.

Variable	Toddler	Children	Adolescents	Young Adults	Adults	Total (N)	*p*
Gender							
Male	5	14	25	28	23	95	0.953
Female	3	11	17	19	17	67	
Symptoms							
Fever	8	23	37	47	39	154	0.186
Pain	0	6	24	28	24	82	< 0.001*
Bleeding	2	7	14	11	13	47	0.876
Nausea/ Vomiting	6	22	35	40	35	138	0.603
Diagnosis							
DF	5	14	27	26	16	88	0.085
DHF	3	11	15	21	24	74	

*sig: $p < 0.05$.

Table 3. Laboratory results based on age category.

Variable	**Age Category** (mean ± SD/ median (min-max)					
	Toddlers	**Children**	**Adolescents**	**Young adults**	**Adults**	***p***
Hemoglobin (g/dL)	12.55 (11.6-18.3)	14.1 (10.8-16.3)	15.6 (12.9-19)	15.29 (11.1-19.2)	15.75 (9.79-25.09)	< 0.001*[a]
Hematocrit (%)	41.77 ± 6.64	40.84 ± 4.74	44.65 ± 4.01	44.74 ± 4.30	44.56 ± 6.04	0.027*[b]
Leukocyte (cell/mm^3)	2,725 (1,800-5,410)	3,260 (1,390-8,190)	2,520 (1,150-6,430)	2,580 (890-7,850)	2,380 (990-8,230)	0.198[a]
Thrombocyte (cell/mm^3)	80,000 (54,000-92,000)	54,000 (16,000-154,000)	40,000 (10,000-96,000)	40,000 (12,000-192,000)	33,500 (8,000-149,000)	0.019*[a]

[a] Kruskal-Wallis analysis; [b] Anova analysis; * Sig: $p < 0.05$.

proportion of cases occurred among males and young adults. In contrast, the evaluation of clinical symptoms by age group showed a significant difference in pain-related complaints ($p < 0.001$) across age groups.

Table 3 presents the laboratory findings classified by age group. Non-parametric variables were analyzed using the Kruskal–Wallis test, which revealed significant differences in hemoglobin levels ($p < 0.001$), hematocrit ($p = 0.027$), and platelet counts ($p = 0.019$) between pediatric and adult patients.

Table 4, analyzed using the Chi-square test, indicates that there is no significant difference in the occurrence of fever, pain, or nausea/vomiting between the DF and DHF groups. However, a statistically significant difference was found in bleeding symptoms, with bleeding occurring more frequently in DHF patients ($p = 0.002$).

Tables 5 and 6 summarize the laboratory findings in relation to DF and DHF diagnoses, as well as gender differences. Table 5 shows that hemoglobin, hematocrit, and platelet levels differed significantly between DF and DHF cases ($p < 0.05$) based on the T-test (parametric analysis) and Mann–Whitney analysis (non-parametric analysis), while leukocyte counts showed no significant difference. Table 6 demonstrates that hemoglobin, hematocrit, and platelet values also varied significantly by gender ($p < 0.05$), whereas leukocyte counts did not show any statistically significant differences.

Table 4. Distribution of gender and symptoms according to diagnosis (DF and DHF).

Variable	DF	DHF	*p*
Gender			
Male	52	43	1.00
Female	36	31	
Symptoms			
Fever	48	48	0.242
Pain	47	35	0.537
Bleeding	16	31	0.002*
Nausea/Vomiting	74	64	0.837

* Sig: $p < 0.05$.

Discussion

In our study, the patients who came to a tertiary hospital with dengue fever (DF) were more commonly diagnosed than DHF, and young adults represented the largest percentage of cases (29%) and were mostly male. These results are consistent with earlier studies by Thai *et al,* which have shown that people between the ages of 20 and 30 are especially susceptible to experiencing dengue [15]. Similarly, a study conducted in China revealed that the greatest number of cases occurred among those between the ages of 25 and 29 [16]. Moreover, several multi-country surveys in Asia have observed a male predominance in dengue incidence among individuals aged ≥15 years [17]. Our study also aligns with a previous study in Surabaya, showing that patients with dengue infection were predominantly male. A study of children aged ≤ 18 years admitted with severe dengue at Dr. Soetomo General Hospital in Surabaya found that of the 48 children, 72.9% were aged 5-12 years, and 58.3% were male [18]. Previous studies conducted in Indonesia have also shown that the age distribution of DHF changes toward older age groups and that specific serotypes are more prevalent in endemic urban areas like Surabaya [19].

In our study, according to Table 2, there are no significant differences in the clinical symptoms between pediatric and adult dengue patients, except in pain reporting. These findings are consistent with previous research conducted by Souza *et al.,* which also reported a significant difference in pain-related symptoms between pediatric and adult dengue patients. This could be due to the difficulty in expressing or characterizing pain in pediatric patients, particularly

Table 5. Laboratory test results based on diagnosis.

Variable	**Diagnosis of Dengue** (mean ± SD/ median (min-max)		
	DF	**DHF**	***p***
Hemoglobin (g/dL)	14.73± 2.03	15.43 ± 1.89	0.027*[a]
Hematocrit (%)	42.9 ± 4.49	45.14 ± 5.44	0.005*[a]
Leukocyte (cell/mm^3)	2,540 (940-8,190)	3,050 (890-8,230)	0.483[b]
Thrombocyte (cell/mm^3)	56,000 (8,000-192,000)	35,000 (8,000-100,000)	0.001*[b]

[a] *t*-test analysis; [b] Mann-Whitney analysis; * Sig: $p < 0.05$.

Table 6. Laboratory test results based on gender.

Variable	**Gender representative** (mean ± SD/ median (min-max)		
	Male	**Female**	***p***
Hemoglobin (g/dL)	15.80 (11.6-19.2)	14.20 (9.79-25.09)	0.000*[a]
Hematocrit (%)	45.54 ± 4.72	41.63 ± 4.64	0.000*[b]
Leukocyte (cell/mm^3)	2,770 (940-8,190)	2,510 (890-8,230)	0.519[a]
Thrombocyte (cell/mm^3)	43,000 (8,000-192,000)	48,000 (8,000-154,000)	0.193[a]

[a] Mann-Whitney analysis; [b] *t*-test analysis; * Sig: $p < 0.05$.

toddlers, and the inability of parents and children to recognize these symptoms. Adults also reported abdominal pain more frequently, possibly due to age-related variations in dengue-affected organs [20,21]. Although statistical analysis revealed no significant difference, our study also revealed that DF infection is more common in adolescents. According to Deng *et al,* compared to older infants, younger newborns may be less susceptible to dengue infection due to a protective level of anti-DENV antibodies from the mother's body. However, compared to older children and adults, initial dengue infections in newborns may have distinct clinical characteristics, progress more quickly into severe forms, and increase the risk of developing into dengue hemorrhagic fever (DHF) and other potentially fatal conditions [22,23].

According to the World Health Organization (WHO), common hematological findings in adult cases of DHF include thrombocytopenia, hemoconcentration, and leukopenia, which are defined as a platelet count of ≤ 100,000 cells/mm³, a hematocrit increase of ≥ 20%, and a white blood cell count of ≤ 5,000 cells/mm³ [5]. In this study, we examined the highest count of hemoglobin and hematocrit level, as well as the lowest count of leukocytes and thrombocytes, in pediatric and adult patients with dengue infection.

Table 3 displayed the variations in hemoglobin and thrombocyte counts between children and adults. According to our study, children's hemoglobin levels were lower than those of adults, and the same was true for thrombocyte levels. This might be because children tend to bleed more than adults do, which lowers their hemoglobin levels [24]. A study by Timan *et al.* indicates that the normal hemoglobin (Hb) levels for children aged 8-12 years range from 11.1 to 14.5 g/dL, with hematocrit (HCT) values between 32.1 and 40.5%. For adolescents aged 13-15 years, Hb levels range from 11.2 to 15.2 g/dL, while HCT values range from 34 to 43.3% [25]. In adults, the reference normal value for hemoglobin (Hb) is 12.73 – 17.6 g/L, and hematocrit (HCT) is 36.54 - 49.3% for males. For females, the normal value for Hb is 10.65-15.36 g/dL, and HCT is 31.8 – 43.4% [26].

Our results showed lower hematocrit levels in children, and so indicated statistically significant differences between the age groups. According to the WHO 2011, both age groups had similar HCT values. The only significant difference was that children with severe dengue had lower HCT levels. Children's lower physiological tolerance to shock, due to their limited cardiac reserve, may be attributed to aggressive intravenous fluid administration or blood resuscitation in response to severe complications [24]. Our result is in line with earlier findings from Pakistan and India that mentioned children are more vulnerable to fast clinical deterioration, whereas adults with comorbid illnesses such as diabetes or renal disease are more likely to develop dengue hemorrhagic fever [3,12,27]. In dengue-endemic areas, these variations highlight the significance of age-specific diagnostic and treatment approaches.

Our study also found that adolescents represented the age group most susceptible to elevated Hb and HCT levels (25.9%) compared with other age groups. The increase in Hb and HCT might reflect plasma leakage, indicating a more severe phase of the disease. Increased microvascular permeability, when allied with the relatively immature hemodynamic compensatory mechanisms in children and adolescents, may account for a higher risk of severe dengue.

In addition, a study by Silva *et al* also showed several independent clinical signs and symptoms associated with severe dengue, such as edema, persistent vomiting, rash, retro-orbital pain, abdominal pain, and a positive tourniquet test. These manifestations are among the well-established warning signs of severe dengue and are important clinical indices used to monitor pediatric and adolescent patients with dengue infection [28].

Our study showed that dengue infection occurred more frequently among adolescents and young adults than adults. Similarly, Deng *et al* reported a shift in the age distribution of dengue infection, which may be attributed to several factors, including limited political commitment, rapid urban population growth, migratory movements, and inadequate financial resources for sustained control efforts [29].

Furthermore, extreme poverty, inadequate sanitation, and climate change have increased the number of *Aedes aegypti* breeding grounds, which has exacerbated the rise in dengue cases. Additionally, Southeast Asia had the highest disability-adjusted life-years (DALYs) burden of dengue infection among children and adolescents, particularly in Indonesia and the Philippines, where dengue DALYs rates (ASDR) were much higher than in other nations. One of the areas most at risk from dengue is Southeast Asia [30].

Another study by Kularatman *et al* mentioned that adults are more likely to have high-severity dengue sickness (DF and DHF) than children [31]. Additionally, adults admitted to the hospital had thrombocytopenia and hemoconcentration that differed markedly from those of children. Children with DHF, which is characterized by enhanced microvascular

permeability, are more likely to have hypovolemic shock than adults; nonetheless, adults infected with the dengue virus had a high fatality rate [32,33].

The classification of DF and DHF was found to be significantly correlated with clinical laboratory results in this study. DF is often considered a mild illness due to its nonspecific symptoms like fever, headache, and pain. In contrast, DHF is a more severe form of dengue characterized by increased vascular permeability and plasma leakage [34]. DHF has a distinct clinical course consisting of three phases: convalescence, critical/leakage, and febrile. During the critical phase, plasma leakage, often presenting as pleural effusion or ascites, can be identified through imaging or decreased serum albumin levels. These conditions can be difficult to identify with a standard physical examination [35].

Compared to DF, DHF is distinguished by more severe bleeding symptoms, such as petechiae, epistaxis, gum bleeding, hematemesis, melena, and a positive tourniquet test. The diagnostic utility of these indicators is demonstrated by the fact that they are substantially more common in DHF (21.1%) than in DF (7.1%). A study by Kalayanarooj *et al* highlights that thrombocytopenia and coagulopathy exacerbate bleeding in DHF, raising the possibility of shock [35]. A study by Juliansen *et al* confirmed that there is a strong correlation between DHF and thrombocytopenia (platelets < 150,000/mm³) and elevated hematocrit levels ($p = 0.002$ and $p < 0.001$, respectively) [36]. DF and DHF are distinct due to plasma leakage, severe bleeding symptoms, hepatomegaly, hemoconcentration, thrombocytopenia, and transfusion requirements. Early identification of these characteristics is crucial in dengue-endemic areas like Indonesia, as it reduces morbidity and mortality. In addition, Rosser *et al* reported a 33% dengue prevalence among children under five in informal urban neighborhoods in Indonesia [37].

Conclusions

This study identified significant differences in clinical laboratory results of dengue infections between adults and children. Children displayed fewer overt discomfort signs, whereas adults commonly reported symptoms like headaches and myalgia. The patterns of thrombocytopenia varied by age group, indicating different disease severity levels. These findings highlighted the necessity for age-specific diagnostic methods to enhance early detection and clinical care.

Authors' Contribution

SUL: Conceptualization, Methodology, Investigation, Data Curation, Supervision, Visualization; LD: Conceptualization, Methodology, Supervision, Investigation, Data Curation; AFA: Methodology, Investigation, Data Curation; AT: Investigation, Data curation, Software; BI: Writing, review, and editing, Project administration; JN: Methodology, Supervision; LSN: Project administration, Writing, and Data collection; ADCN: Project administration, Writing, and Data collection; RPA : Project administration, Visualization.

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Conflict of interest

No conflict of interest is declared.

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