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The relationship of leukocyte number and plattle number in patients with dengue fever (DHF) at Puskesmas Piyungan

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Abstract
Background: Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by the dengue virus. Dengue fever is transmitted by Aedes aegypti and Aedes albopictus mosquitoes. In dengue fever sufferers, when a complete blood test is performed, the most common result is a decrease in the number of leukocytes and the number of platelets. *Objectives*: This study aims to determine the relationship between the number of leukocytes and platelets in DHF patients at Puskesmas (primary health center) Piyungan. *Materials and Methods*: The type of research used was analytical observational with a cross sectional research design and the data were collected using total sampling techniques. Data was obtained from medical records with a sample size of 26 patients. The relationship between the number of leukocytes and the number of platelets in dengue fever sufferers was tested using the Spearman's correlation test. *Results*: The result of analysis using the Spearman's correlation test did not show a significant relationship between the number of leukocytes and the number of platelets in dengue fever patients (p = 0.0774), and the level of relationship was very weak with a positive relationship direction (r = 0.059). *Conclusions*: there was no significant relationship between the number of leukocytes and the number of platelets in dengue fever patients at Puskesmas Piyungan. A decrease in the number of leukocytes and platelets is a common condition that is often found in dengue fever patients.

Keywords
DHF, Leukocytes, Trombocytes.

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1. Introduction

Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by the Dengue virus. Dengue fever is transmitted through the bites of Aedes aegypti and Aedes albopictus mosquitoes. Until now, dengue fever is still a health problem in the world because it can cause high mortality (Yushananta, 2021). This disease is very dangerous and deadly, so it must be treated immediately (Marisa & Suriani, 2019).

Based on data from the Ministry of Health of the Republic of Indonesia, dengue fever cases in Indonesia in 2021 were 73,518 cases with a total of 705 deaths. DHF cases in the Special Region of Yogyakarta (DIY) are in 12th place with a morbidity rate of 29.9 per 100,000 population (Kemenkes RI, 2022). From DIY Province, the highest cases were in Bantul Regency with 410 cases, and the lowest cases were in Yogyakarta City with 93 cases. The highest dengue fever cases in the Bantul area occurred in Piyungan District (Dinkes, 2022).

DHF generally begins with symptoms of sudden high fever lasting 2-7 days (38-40°C), bleeding, conjunctiva, epistaxis, melena, hepatomegaly, shock, thrombocytopenia, hemoconcentration, bleeding from the gums, severe headache, pain behind the eye muscles. and joints, decreased appetite, nausea, and rash. Dengue fever appears suddenly and can spread quickly in a very short time. This disease is very dangerous and deadly so it must be treated immediately (Marisa & Suriani, 2019).

Laboratory examination is one of the supporting examinations used to diagnose dengue fever (Joharsah et al., 2021). The most common results in a complete blood test are a decrease in the number of leukocytes (leukopenia) and the number of platelets (thrombocytopenia) (Syafutra et al., 2022). Leukocytes or white blood cells are blood components produced by hemopoetic tissue (granulated leukocytes) and lymphatic tissue (non-granulated leukocytes). The normal number of leukocytes in the body is around 4,000-11,000/mm3 (Prasthio et al., 2022). A decrease in the number of leukocytes or leukopenia occurs in cases of dengue fever. Leukopenia occurs on the first and third days of fever, this is caused by the degeneration of mature polymorphonuclear (PMN) cells and the formation of young PMN cells (Syafutra et al., 2022). Platelets or platelets are fragments of the cytoplasm of megakaryocytes formed by the bone marrow. Platelets are blood cells that have a small specific gravity and do not have a nucleus. Platelets have a lifespan of around 1-2 weeks or 8 days. The normal platelet count is around 150,000-450,000/mm3. A decrease in the number of platelets or thrombocytopenia occurs on the third to seventh day in DHF sufferers. The decrease in the number of platelets is caused by the mechanism of bone marrow suppression, platelet destruction, and shortening of the life span of platelets (Syafutra et al., 2022).

Research conducted by Aprilia (2022) at the Aulia Husada Inpatient Clinic in Bogor resulted in results showing that there was no significant relationship between the number of leukocytes and the number of platelets in dengue sufferers. These results are different

from research conducted by Rosidah & Fauziyah (2016) at Haji Hospital Surabaya regarding the relationship between platelet levels and leukocytes in dengue fever patients. It can be concluded that there is a relationship between the number of platelet levels and the number of leukocyte levels in dengue fever patients.

Based on several studies, it can be concluded that research on the relationship between the number of leukocytes and the number of platelets in dengue fever patients has been carried out several times, but the results reported are inconsistent. This attracted researchers' interest in finding out whether there was a relationship between the number of leukocytes and the number of platelets in dengue fever patients at the Piyungan Community Health Center.

2. Materials and Methods

The type of research used was analytical observational with a cross sectional research design to determine the relationship between leukocyte counts and platelet counts in dengue fever patients. This research was conducted in the medical records section of the Piyungan Health Center. Data was taken from medical records of dengue fever patients for the period January 2021 – December 2022. The population of this study was all dengue fever patients who underwent hematology laboratory examinations at the Piyungan Community Health Center. The samples used were dengue fever patients who met the inclusion and exclusion criteria. Inclusion criteria were dengue fever patients from January 2021 – December 2022 who had a hematology examination and had leukocyte and platelet results. Exclusion criteria are dengue fever patients who have incomplete medical record data and suffer from other diseases that cause disturbances in the number of leukocytes and platelets. Diseases that cause disturbances in the number of leukocytes and platelets are anemia and HIV. This research was carried out after submitting an ethical permit with number No.1766/KEP-UNISA/VII/2023.

3. Results and Discussion

3.1. Results

Research conducted at the Piyungan Community Health Center obtained medical record data for 26 samples that met the research inclusion criteria.

Table 1. Characteristics of DHF sufferers based on age and gender

Sample Characteristics	F	Percentage (%)
Age (year)		
0-17	20	76,9
18-65	6	23,1
66-79	0	-
80-99	0	-
>100	0	-
Gender		
Male	10	38,5
Female	16	61,5

Based on table 1, it shows that most dengue fever patients occur in children aged 0-17 years, namely 20 patients (76.9%). DHF most often affects female patients, 16 people (61.5%).

Table 2. Frequency of leukocyte counts in DHF patients

Number of Leukocytes	Frequency	Percentage (%)
<4.000/mm3	15	57,7
4.000-11.000/mm3	9	34,6
>11.000/mm3	2	7,7
Total	26	100

Based on table 2, it shows that on a complete blood count of leukocyte parameters, most dengue fever patients had a leukocyte count <4,000/mm3 with 15 patients (57.7%).

Table 3. Frequency of Platelet Counts in DHF Patients

Platelet Count	Frequency	Percentage (%)
<150.000/mm3	15	57,7
150.000-450.000/mm3	11	42,3
>450.000/mm3	-	-
Total	26	100

Based on table 3, it shows that on a complete blood count of platelet parameters, most dengue fever patients had platelet counts <150,000/mm3, 15 patients (57.7%).

Table 4. Relationship between the number of leukocytes and the number of platelets in dengue fever patients

Leukocyte	Platelet				P-value	Correlation Coefficient(r)
	Low (F)	Normal (F)	Height (F)	Total		
Low (F)	9	6	0	15		
Normal (F)	5	4	0	9	0,774	0,059
Height (F)	1	1	0	2		
Total	15	11	0	26		

Based on table 4, a Spearman's correlation test was carried out and the probability value (p-value) was 0.774, which means >0.05, and the correlation coefficient (r) was 0.059. These results stated that there was no significant relationship between the number of leukocytes and the number of platelets.

3.2. Discussions

Dengue Hemorrhagic Fever is a disease that is still a health problem in the world because it can cause high mortality (Yushananta, 2021). Dengue fever most often occurs in children and women. The reason children are more likely to get dengue fever is because of activities outside the home which have the chance of being infected with the dengue virus (Mardhatillah et al., 2020). Children's immature immune system is also one of the reasons why children are more susceptible to dengue fever. Children who lack nutritional status will be susceptible to dengue virus infection because they have low cellular immunity, which can cause immunological memory and immune responses to not develop properly (Ramayani et al., 2022). Insufficient formation of specific antibodies (CD4+ and CD 8+ T-helper cells) can also cause interferon (IFN) production by macrophages to be unable to slow down the replication and spread of infection (Tansil et al., 2021).

Women are more susceptible to dengue fever because women's immune systems are low (Idris & Zulaikha, 2021). Women who are underweight and have low cellular immunity can cause immune reactions and immunological memory to not develop properly. Poor health conditions can cause a decrease in immunity, a decrease in the number of T-helper cells, as well as disruption of phagocytosis and imperfect immunological memory, so that T-helper lymphocytes as the body's immune response cannot produce cytokines and

mediators that are used as protection and defense of the body (Wahidin, 2022).

The role of leukocytes when exposed to dengue fever occurs in blood circulation. Dengue viruses that enter the bloodstream will be captured by macrophages. Macrophages then process the dengue virus so that the macrophages become APC (antigen presenting cells). APCs that attach to macrophages will activate T-Helper cells and attract other macrophages to phagocytize more viruses. T-Helper cells will activate T-cytotoxic cells which will then lyse macrophages that have phagocytosed the virus. This causes dengue sufferers to experience leukopenia or leukocystosis (Hidayat et al., 2021).

A normal leukocyte count in dengue infection occurs because it is possible that the patient's condition when taken to a health facility already had a fever on the fifth day when the leukocyte count had returned to normal. Leukocytosis in DHF occurs due to secondary infection or bleeding reactions. Secondary infections caused by bacteria can be the cause of death in dengue cases. A high leukocyte count can also be used as a warning sign that dengue infection is getting worse (Rahmadiani, 2021).

The decrease in the number of platelets in dengue fever patients is due to a decrease in platelet production due to bone marrow suppression due to direct viral infection of hematopoietic progenitor cells and stromal cells. There is an increased consumption of platelets which are used to repair vascular damage. There is increased destruction due to antibodies produced during dengue virus infection showing cross-reaction with several self-antigens (platelets) causing platelet lysis (Arifa et al., 2018). Thrombocytopenia is one of the laboratory results for diagnosing dengue fever, however, in some cases there is a normal or even higher platelet count. The normal platelet count in DHF is caused by the fact that on the fifth to eighth day of the disease, there is an increase in young megakaryocytes so that the platelets will return to the normal limit of platelet count (Kamila et al., 2022).

There was no significant relationship between the number of leukocytes and the number of platelets in dengue fever patients because the p-value was 0.774. These results are supported by research conducted by Aprilia (2022) where the results showed that there was no correlation between the number of leukocytes and the number of platelets in children with dengue fever.

Leukopenia occurs from the first day of fever to the third day which is caused by the

degeneration of mature polymorphonuclear (PMN) cells and the formation of young PMN cells. Thrombocytopenia occurs on the third to seventh day which is caused by mechanisms of bone marrow suppression, platelet destruction, and shortening of the life span of platelets. Platelets will return to normal on the eighth or ninth day (Syafutra et al, 2021).

Complete Blood Examination at the Piyungan Community Health Center using a Hematology Analyzer. The Hematology Analyzer tool used uses the impedance method. The weakness of the impedance method is that there is a possibility that two cells can pass through the gap simultaneously, besides that cells that have been measured can return to measurement, resulting in the cells being counted twice by the detector (Wulandhari, 2020). If erythrocyte cells experience disintegration, the cells will swell. This causes the size of erythrocyte cells to be almost the same as leukocyte cells, so they will be read as leukocyte cells on the Hematology Analyzer (Aisyah, 2018).

Factors that can cause a decrease in the number of leukocytes and platelets are delays in blood tests (Fiani, 2021). Blood samples for checking the number of leukocytes, if stored at room temperature, must be examined in less than two hours. Examination carried out for more than two hours will cause degeneration of leukocyte cells so that leukocyte results that should be high become falsely low (Aisyah, 2018). Blood samples to check platelet counts must be done immediately with a delay of one hour. Delaying the examination can cause platelets to cluster and swell, forming fragments with a smaller size so that they cannot be read as platelets on the Hematology Analyzer (Puspitasari et al., 2022).

The use of anticoagulants also needs to be considered in a complete blood count. The use of inappropriate anticoagulants such as heparin is not recommended for complete blood tests because it can cause blood cells to clot and result in invalid calculations (Fitria et al., 2016). The anticoagulant EDTA (Ethylenediaminetetraacetic Acid) is the most widely used anticoagulant for complete blood tests. EDTA anticoagulant can maintain blood cell structure and prevent platelet aggregation (Yolanda, 2022).

4. Conclusions

There was no significant relationship between the number of leukocytes and the number of platelets in dengue fever patients at the Piyungan Community Health Center. Low or

normal leukocyte counts and a decrease in platelet counts are common conditions that are often found in dengue fever patients.

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Author Contributions: ARRD, ANR, TDA: designed the study. ARRD: data collection, data analysis, and manuscript preparation. ANR, TDA: revised the manuscript. All authors read and approved the final version of the manuscript.

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