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Correlation Between Leukocyte and Platelet Counts and NS-1 Antigen Results in Patients with Suspected Dengue Hemorrhagic Fever

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ABSTRACT

Dengue Hemorrhagic Fever (DHF) remains a significant global health concern, with severe cases contributing to high morbidity and mortality worldwide. Leukopenia and thrombocytopenia are frequently observed in dengue patients, and early detection using NS-1 antigen testing is essential due to its high sensitivity in the initial phase of infection. Reductions in leukocyte and platelet counts can serve as indicators of disease severity and assist in the diagnosis of DHF. This cross-sectional observational study aimed to evaluate the relationship between total leukocyte and platelet counts and NS-1 antigen results in patients with suspected DHF. A total of 91 patients attending Mayong II Health Center, Jepara, from January to December 2024 were included through total sampling. Results indicated that males were the predominant group, with 62% aged 0–5 years. The mean leukocyte count was 12,457 ± 3,471 cells/mm³ (range: 3,400–20,500), and the mean platelet count was 162,626 ± 72,930 cells/mm³ (range: 54,000–385,000). NS-1 antigen testing was positive in 69% of patients. Spearman's rank correlation analysis demonstrated no significant association between leukocyte counts and NS-1 results ($p = 0.220$), whereas a significant correlation was observed between platelet counts and NS-1 results ($p < 0.001$). These findings highlight that platelet counts are significantly associated with early dengue virus detection via NS-1 antigen and may serve as a valuable supportive marker in diagnosing DHF. Routine monitoring of platelet counts could facilitate timely identification and management of patients at risk for severe dengue.

INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by the dengue virus, transmitted primarily by Aedes aegypti and Aedes albopictus mosquitoes (Devina, Rimbun, and Situmeang 2022). This disease remains a major public health concern due to its potential to cause severe complications and death (Candra 2016). National data from the Indonesian Ministry of Health reported a case fatality rate of 0.8% in 2023 (Kemenkes RI 2024). In Central Java Province, 6,157 cases and 144 deaths were recorded with a mortality rate of 2.2% (Dinkes Prov Jateng 2023). Jepara District documented 129 cases with a mortality rate of 3% in 2023 (Dinkes Kabupaten Jepara 2023), while Mayong II Public Health Center reported 50 cases, including 22 confirmed DHF and a mortality rate of 4% (Dinkes Kabupaten Jepara, 2024). In early 2024, the number of DHF cases in Jepara District increased significantly, reaching 507 cases by February 22, with 1.7% resulting in death. This surge prompted the local government to declare a non-natural emergency status for DHF through Decree No. 360/48 of 2024, later extended until March 18, 2024 (Dinkes

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Kabupaten Jepara 2024). This situation highlights the continued potential for DHF to cause outbreaks if not managed promptly and effectively (Kemenkes RI 2022).

Diagnosis of DHF follows WHO recommendations, relying on both clinical and laboratory assessments (Marsudi, Irwadi, and Sumbung 2022). Hematological parameters, particularly leukocyte and platelet counts, play a crucial role in evaluating disease progression. Leukopenia and thrombocytopenia are common findings among DHF patients and may indicate the severity of infection (Syafutra, Almurdi, and Syah 2022). Leukopenia is associated with bone marrow suppression and immune response to viral infection, whereas thrombocytopenia results from decreased platelet production and increased destruction mediated by immune mechanisms (Hidayatullah and Aisyah 2018). In addition to hematological examination, detection of dengue nonstructural protein-1 (NS-1) antigen is essential for early diagnosis. NS-1 demonstrates high sensitivity during the acute phase, particularly within the first 0–3 days of fever (Santosa 2020). This test can detect up to 77% of suspected DHF cases (Sari and Yasa 2020) and is especially valuable before thrombocytopenia occurs or before IgM antibodies are detectable (Sari, Natalia, and Parinding 2020).

Previous studies have reported associations between NS-1 antigen results and alterations in leukocyte and platelet counts during the early phase of dengue infection (Wulandari, Hadi, and Eka Putri 2023). Progressive leukopenia typically appears between days 3 and 8 of fever, followed by thrombocytopenia and hemoconcentration (Wila and Nusa 2020). Severe thrombocytopenia is strongly linked to bleeding manifestations, a major complication of DHF (Hidayat, Yaswir, and Murni 2017). Other studies have also identified significant correlations between leukocyte and platelet counts in both primary and secondary dengue infections Syafutra *et al.*, 2022).

Routine monitoring of hematological parameters provides valuable information for clinical management and supports timely therapeutic decision-making (Masihor et al. 2013). Therefore, examining the relationship between leukocyte count, platelet count, and NS-1 antigen results is essential to strengthen early diagnostic strategies and improve DHF case management. Based on these considerations, this study aims to analyze the relationship between leukocyte and platelet counts and NS-1 antigen results among suspected DHF patients at Mayong II Public Health Center.

MATERIALS/METHOD

A quantitative analysis was used as the research methodology, with an observational design and a cross-sectional perspective. The study population consisted of data from all patients with suspected dengue hemorrhagic fever (DHF) at the Mayong II Health Center who presented with febrile symptoms for 1 to 3 days between January and December 2024. A total of 91 samples were collected using a comprehensive sampling technique. Inclusion criteria were all patients with suspected DHF who had complete laboratory records, including leukocyte, platelet, and NS-1 antigen results. Exclusion criteria included patients with incomplete laboratory data, comorbid conditions affecting leukocyte or platelet counts, or patients who were referred to other facilities during the study period. The research was conducted at the Mayong II Health Center, Jepara, between January and March 2025. Ethical license number 156/EA/F.XXIII.38/2025 was issued by the Research Ethics Committee of the Semarang Polytechnic Institute of the Ministry of Health. Secondary data collection methods were employed in this study. The secondary data used is medical record data of suspected DHF at Mayong II Health Center in 2024. Data were sorted and collected using an observation sheet. The data on the observation sheet was then transferred into a master

table format. The data obtained were presented in tabular form. Univariate and bivariate analysis used IBM Statistics SPSS 25.0.

RESULTS AND DISCUSSION

1. Characteristics Patient Dengue Fever Suspect
   Study implemented at the Community Health Center Mayong II in January -March 2025. Sampling technique in study use method *total sampling* with amount patient dengue fever suspects during 2024 which will be sample study is 91 patients with characteristics presented in Table 1.

Table 1 Characteristics subject research (n=91)

Variables	Gender				Total	
	Man		Woman			
	n	%	n	%	n	%
Age						
Toddlers (0-5 years)	28	62%	17	38%	45	100%
Children (6-11 years)	12	52%	11	48%	23	100%
Teenagers (12-25 years)	13	77%	4	23%	17	100%
Adults (26-45 years)	2	50%	2	50%	4	100%
Elderly (≥ 46 years)	1	50%	1	50%	2	100%
Total	56	62%	35	38%	91	100%

Based on Table 1, there are 52 patients suspected dengue fever sex men (62%), with amount most originate from group age toddlers (0-5 years) as many as 62%. Based on research that has been carried out at the Community Health Center Mayong II, patient 62 % of suspected DHF cases are of the same type sex men . Research by (Rao et al. 2024; Wila and Nusa 2020) give results similar that more dengue fever infections Lots occurs in men than women . Men tend own response more immunity weak to viral infections compared Woman Because production more cytokines low and more efficient low in produce immunoglobulins and antibodies . In contrast , women own hormone estrogen which can increase synthesis of IgG and IgA, providing protection addition to infection viruses such as dengue (Ashary et al., 2024) . System mobility man more often go out House compared to with women , so that more big risk infected (Maulin & Irma, 2023) . Age patient Dengue fever suspects are dominated by age toddlers 0-5 years (62%) and children (6-11 years) as much as 52%. This matter in line with study (Efiariza et al. 2023) that group age most in pediatric DHF patients be in range ages 2-11 years with type sex male . Dengue virus replicates in cells endothelium blood . Toddlers up to children own endothelium more vascular permeable and thinner than in vulnerable adults to dengue virus replication , if increased viral virulence can increase severity disease (Widarti et al., 2023) . Severity dengue hemorrhage can become factor predictive length of stay hospitalization of patients child with dengue fever. The severity of dengue fever can determined based on age (Ikrima et al., 2017) .

2. Amount Leukocytes Patient Dengue Fever Suspect
   Average number leukocytes patient dengue fever suspect at the community health center Mayong II is 12,457±3,471 cells /mm ^{3} . Examination results amount leukocytes highest 20,300 cells /mm ^{3} and lowest is 3,400 cells /mm ^{3} blood . Leukocyte data classified into 3 categories , namely normal leukocytes : 4000-11,000 cells / ^{mm3} blood ,leukopenia: <4000 cells / ^{mm3} blood and leukocytosis : >11,000 cells / ^{mm3} blood . Examination results Friday leukocytes categorized based on type sex presented in Table 2.

Table 2 Total Leukocytes Based on Subject Patient Gender Characteristics Dengue Fever Suspects (n=91)

Characteristics	Patient Dengue Fever Suspect							
	Normal Leukocytes		Leukocytosis		Leukopenia		Total	
	n	%	n	%	n	%	n	%
Gender								
Man	4	7%	50	89%	2	4%	56	100%
Woman	5	14%	25	72%	5	14%	35	100%
Total	9	10%	75	82%	7	8%	91	100%

Leukocytosis results occurs most frequently in patients male dengue fever suspect as much as 89%. Examination results Friday leukocytes categorized based on age in Table 3.

Table 3 Total Leukocytes Based on Characteristics Age Subject Patient Dengue Fever Suspects (n=91)

Characteristics	Patient Dengue fever suspect							
	Normal Leukocytes		Leukocytosis		Leukopenia		Total	
	n	%	n	%	n	%	n	%
Age								
Toddlers (0-5 years)	5	11%	39	87%	1	2%	45	100%
Children (6-11 years)	3	13%	16	70%	4	17%	23	100%
Teenagers (12-25 years)	0	0%	16	94%	1	6%	17	100%
Adults (26-45 years)	1	25%	3	75%	0	0%	4	100%
Elderly (≥ 46 years)	0	0%	1	50%	1	50%	2	100%
Total	9	10%	75	82%	7	8%	91	100%

Leukocytosis was observed in 82% of patients across all age groups, with the highest prevalence in toddlers (0–5 years, 87%). This finding deviates from the classical dengue presentation, which typically features leukopenia, and aligns with previous reports that dengue patients without shock may initially have normal leukocyte counts, followed by an increase by day three. Several factors may explain this atypical pattern: secondary infection (including bacterial co-infection), timing of sample collection, and potential misclassification of suspected DHF cases. Leukocytosis may also result from a bleeding response and can serve as an early warning for severe dengue (Widarti et al., 2023) Individual immune responses vary, highlighting heterogeneity in hematological presentation among dengue patients (Rosyanti & Hadi, 2020).

3. Amount Platelets Patient Dengue Fever Suspect

Average number platelets patient dengue fever suspect at the community health center Mayong II is 162,626±72,930 cells /mm ^{3} blood . Amount platelets highest 385,000 cells / ^{mm3} blood and the lowest 54,000 cells /mm ^{3} blood . Platelet data classified into 2 categories that is Normal platelets : 150,000-450,000 cells / ^{mm3} blood and platelets abnormal (thrombocytopenia): <150,000 cells / ^{mm3} blood . Examination results Friday platelets categorized based on type sex presented in Table 4.

Table 4 Total Platelets Based on Subject Patient Gender Characteristics Dengue Fever Suspects (n=91)

Characteristics	Patient Dengue Fever Suspect					
	Normal Platelets		Thrombocytopenia		Total	
	n	%	n	%	n	%
Gender						
Man	27	48%	29	52%	56	100%
Woman	10	29%	25	71%	35	100%
Total	37	41%	54	59%	91	100%

Thrombocytopenia results patient DHF suspects occurred mostly in 29 patients man or by 52%. The results of the examination Friday platelets categorized based on age served in Table 5.

Table 5 Total Platelets Based on Characteristics Age Subject Patient Dengue Fever Suspects (n=91)

Characteristics	Patient Dengue Fever Suspect					
	Normal Platelets		Thrombocytopenia		Total	
	n	%	n	%	n	%
Age						
Toddlers (0-5 years)	18	40%	27	60%	45	100%
Children (6-11 years)	11	48%	12	62%	23	100%
Teenagers (12-25 years)	6	35%	11	65%	17	100%
Adults (26-45 years)	1	25%	3	75%	4	100%
Elderly (≥ 46 years)	1	50%	1	50%	2	100%
Total	37	41%	54	59%	91	100%

Thrombocytopenia results happens all over group age with group age patient most dengue fever suspects happen age toddlers 0-5 years by 60% or as many as 27 patients. Patient dengue fever suspect in study This 41% have normal platelets and 59% thrombopenia. This in line with study (Hidayatullah & Aisyah, 2018) which states the average number of platelets patient infected with dengue virus is low below 100,000 cells / mm^3 blood . Decrease amount platelets become the most common picture found in DHF patients , the more low platelets so the severity of dengue fever is increasing increase (Maulin & Irma, 2023) . Thrombocytopenia is characteristics typical from dengue fever, where the virus can cause damage to the spinal cord bones and affects production platelets. Decrease amount platelets is one of the factor important prognostic in evaluate severity of DHF (Huy & Toàn, 2022) . Infected platelets will Lots damage normal platelets so that amount platelets will decreased and there is destruction excess platelets in the periphery so that will risky occurrence bleeding in DHF patients . Production platelets in the bone marrow bones also become hampered consequence dengue virus induction so that amount platelets also participate down (Widarti et al., 2023) .

4. Patient NS-1 Results Dengue Suspect

Based on type gender , results NS-1 examination was obtained results most positive in patients male . The results of the NS-1 examination are categorized based on type sex presented in Table 6.

Table 6 NS-1 Examination Results Based on Subject Patient Gender Characteristics Dengue Fever Suspects (n=91)

Characteristics	NS-1 Results					
	Positive		Negative		Total	
	n	%	n	%	n	%
Gender						
Man	35	63%	21	37%	56	100%
Woman	28	80%	7	20%	35	100%
Total	63	69%	28	31%	91	100%

The results of the NS-1 examination were obtained results positive in 35 patients man with percentage 63%. The results of the NS-1 examination are categorized based on age served in Table 7

Table 7 NS-1 Results Based on Characteristics Age Subject Patient Dengue Fever Suspects (n=91)

Characteristics	NS-1 Results					
	Positive		Negative		Total	
	n	%	n	%	n	%
Age						
Toddlers (0-5 years)	31	86%	14	14%	45	100%
Children (6-11 years)	15	65%	8	35%	23	100%
Teenagers (12-25 years)	13	76%	4	24%	17	100%
Adults (26-45 years)	3	75%	1	25%	4	100%
Elderly (≥ 46 years)	1	50%	1	50%	2	100%
Total	63	69%	54	31%	91	100%

The results of the NS-1 examination were obtained results most positive occurs in groups age toddlers 0-5 years by 86%. The results of the NS-1 examination presented in tables 4.6 and 4.7, obtained patient NS-1 results positive dengue fever suspect as much as 69%. This is in harmony with research that shows that The NS-1 tool has sensitivity ranges from 63%-93.4% with specificity 100% then positive NS-1 result truly occurs in people infected with the dengue virus as well on the contrary (Santosa, 2020) . NS-1 antigen examination can done on the day First because of the circulating protein circulate with concentration tall in blood patients at the beginning infection acute and will decreased on the day to 5-6. NS-1 examination can detect part from dengue virus body so that No need wait response body to viral infection . This is prove that NS-1 can used as indicator beginning dengue infection . NS-1 antigen is a very useful marker in the diagnosis of DHF in the phase beginning infection . Detection of NS-1 antigen can improve early diagnosis of dengue fever, so that allows more interventions fast (A. Joshi et al., 2017) .

The examination results also showed that 31% of patients dengue fever suspects show the most negative NS -1 results were in the group age toddlers (0-5 years) and children (6-11 years). According to (Raihan et al. 2025) NS-1 negative cases more general occurs in children (0–15 years), which indicates that maturity immunity and exposure previously affects NS-1 antigenemia. NS-1 sensitivity is general more high in primary infections , but in children can experience cleaning immune early , so that in case of infection secondary cause more Lots results negative false . In cases of severe dengue fever in children , the presence of complex immune can reduce ability detectability of NS-1 so that important perform diagnostic tests alternative in case pediatric NS-1 negative For prevent missed dengue fever diagnosis in children .

5. Relationship Amount Leukocytes with NS-1 Results

Based on the *Spearman* test , it was found that *p value* = 0.220>0.05 so H0 is accepted , which means that No There is significant relationship between amount leukocytes with NS-1 results in patients. Study This prove that No There is connection between amount leukocytes with NS-1 results in patients . Research This in line with study performed by Zida Maulina et al (2016) about connection average results inspection laboratory to degrees clinical dengue virus infection in patients children at Santa Anna Hospital, that no connection between average amount leukocytes to clinical DHF (Devina et al., 2022) . The number of Leukocytes in dengue infection are usually normal or decreasing and sometimes happen leukocytosis moderate . Leukopenia in a number of case dengue infection is caused by Because existence destruction or inhibition (inhibition) in produce cells leukocytes in the bone marrow triggered bone Because existence viral infection . Decrease leukocytes usually happened at the time beginning fever and will down return moment before fever start

down or end (Widarti et al., 2023) . Research results interesting Because show that leukocytosis No always related direct with dengue infection . Leukocytosis accompanied by fever also becomes indicator existence infection or inflammation in body as in fever typhoid (Aeni & Saptaningtyas, 2023) , infection channel breathing on (Hikma et al., 2023) and cancer (Yanuar et al., 2024) . Leukocytosis also occurs in one third of patient tuberculosis lungs (Alamlih et al., 2020) . Leukocytosis accompanied by fever can found in inflammatory Bowe's disease (De Simone et al., 2021) .

6. Relationship Amount Platelets with NS-1 Results

Spearman's rank correlation analysis showed a very strong negative correlation between platelet counts and NS-1 antigen results ($r = -0.772$, $p < 0.001$), indicating that H_0 was rejected. Clinically, this means that patients with lower platelet counts are more likely to test positive for NS-1, reflecting active dengue virus infection. The negative direction of the correlation suggests an inverse relationship: as platelet counts decrease (thrombocytopenia), NS-1 positivity increases. This finding reinforces previous studies (Andrew O. et al., 2016; Rosdiana, 2017; Rika Mayasari et al., 2019; Devina et al., 2022), which reported that declining platelet counts are closely associated with the clinical severity of DHF patients (Devina et al., 2022) . The platelet decline is also linked to plasma leakage, a consequence of immune reactions between the virus and the host immune system, which can alter vascular integrity and facilitate viral penetration into blood vessels (Paizer et al., 2024) (Paizer et al., 2024). Overall, monitoring platelet counts may serve as a practical early indicator of dengue virus activity and help identify patients at risk for severe DHF.

CONCLUSIONS

Based on the results, there is no significant association was observed between leukocyte counts and NS-1 antigen results among suspected DHF patients; however, a significant association was identified between platelet counts and NS-1 antigen results at Mayong II Public Health Center. Further clinical evaluation is warranted for suspected DHF patients with negative NS-1 antigen results, as alternative diagnoses cannot be excluded.

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