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# Factors Related to the Severity of Dengue Infection in Adult Patients Treated at Sanjiwani Regional General Hospital

Ida Bagus Made Agastya Pranata[1], Saraswati Laksmi Dewi[2], Putu Aryagiri Prebawa[2], Komang Trisna Sumadewi[3*]

1. Faculty of Medicine and Health Sciences, Universitas Warmadewa, Bali, Indonesia
2. Department of Internal Medicine, Faculty of Medicine and Health Sciences, Universitas Warmadewa, Bali, Indonesia
3. Department of Anatomy, Faculty of Medicine and Health Sciences, Universitas Warmadewa, Bali, Indonesia

Correspondence:
Ida Bagus Made Agastya Pranata
trisna_sumadewi@yahoo.com

**Abstract**
Dengue infection remains a major global health problem. This study aimed to determine factors associated with the severity of dengue infection among adult patients treated at Sanjiwani Gianyar Regional General Hospital in 2023. An analytical observational study with a cross-sectional design was conducted using consecutive sampling. A total of 100 adult patients with confirmed dengue infection were included. Severity was classified as Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) based on WHO criteria. Chi-square analysis and crude odds ratio (OR) estimation were performed. Age >60 years was significantly associated with severe dengue (OR = 2.94; 95% CI: 1.25–6.92; p=0.014). Female gender was also associated with higher odds of severe dengue compared to males (OR = 2.33; 95% CI: 1.05–5.15; p=0.039). Secondary infection status showed the strongest association with severity (OR = 5.40; 95% CI: 2.24–13.04; p=0.001). In conclusion, age, gender, and infection status were significantly associated with dengue severity. These findings may assist clinicians in identifying patients who require closer clinical monitoring.

**Keywords:** dengue fever; dengue hemorrhagic fever; dengue virus

## Introduction

Dengue virus (DENV) infection remains a significant public health problem in tropical and subtropical regions, with an estimated 390 million infections occurring annually worldwide, of which approximately 96 million manifest clinically.[1] The disease is transmitted primarily by Aedes aegypti and Aedes albopictus mosquitoes, and Indonesia is classified as a hyperendemic country with sustained high transmission rates.[2–4]

Data from the Bali Provincial Health Office showed fluctuating but consistently high dengue incidence from 2020 to 2023, with a significant increase observed in 2020 reaching 137.3 per 100,000 population compared to 22.4 per 100,000 in the previous year. As one of Indonesia's major tourism destinations, Bali continues to face substantial risk of dengue transmission due to population mobility, urban density, and environmental factors favorable to mosquito breeding. In addition to dengue, Bali has also reported other infectious diseases, including human immunodeficiency virus (HIV), Japanese encephalitis, and malaria, which further highlight the infectious disease burden in the region.[5,6] The peak incidence of

dengue cases typically occurs between February and June each year[2,3].

Although dengue infection is often self-limiting, some patients develop severe manifestations such as dengue hemorrhagic fever (DHF) and dengue shock syndrome, which can lead to significant morbidity and mortality. Identifying factors associated with disease severity is therefore crucial for improving early recognition and clinical management.

This study aims to determine the factors associated with the severity of dengue virus infection among adult patients treated at Sanjiwani Gianyar Regional General Hospital in 2023. The study focuses on the relationships among age, gender, infection status, and disease severity. Understanding these associations is expected to contribute to better clinical risk stratification and provide a reference for further research on dengue infection.

## Material and methods

This study was an analytical observational study with a cross-sectional design conducted at Sanjiwani Regional General Hospital, Gianyar, Indonesia, from January 1 to December 31, 2023. The study aimed to identify factors associated with the severity of dengue virus infection in adult hospitalized patients. The target population consisted of all patients hospitalized with dengue infection during the study period. The accessible population included adult patients aged ≥18 years who met the inclusion criteria. The sample was obtained using a consecutive sampling technique. A minimum sample size of 96 was calculated using a 95% confidence level and an estimated proportion of dengue severity from previous studies. A total of 100 patients met the eligibility criteria and were included in the final analysis. Inclusion criteria were adult patients (≥18 years) with confirmed dengue infection. Patients with documented comorbidities such as hypertension and diabetes mellitus were excluded to minimize potential confounding effects.

Dengue infection was confirmed based on positive laboratory results recorded in the medical records, including NS1 antigen and/or dengue IgM/IgG serological testing.

Severity classification followed the World Health Organization (WHO) 1997 criteria, categorized into Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) grades I–IV. For inferential statistical analysis, severity was dichotomized into Non-severe dengue (DF), Severe dengue (DHF grades I–IV). Primary infection was defined as positive dengue IgM with negative IgG serology. Secondary infection was defined as positive IgG with or without IgM positivity during the acute phase. The independent variables included age (categorized as <60 years and ≥60 years), gender (male/female), and infection status (primary/secondary). The dependent variable was dengue severity (DF vs DHF).

Patients with incomplete medical records for key study variables were excluded from the analysis. No missing data were identified in the final dataset. Data were analyzed using SPSS version XX. Descriptive statistics were used to summarize patient characteristics. Categorical variables were analyzed using the Chi-square test to assess associations between independent variables and dengue severity. Crude odds ratios (OR) with 95% confidence intervals (CI) were calculated to estimate the strength of association. Since multivariable logistic regression was not performed, the reported associations represent unadjusted estimates. Statistical significance was defined as $p < 0.05$.

## Results

The results showed that among 100 patients with confirmed dengue virus infection treated at Sanjiwani Gianyar Regional General Hospital, most respondents were male (52.0%), with an average age of 52.24 ± 12.71 years, and 64.0% were under 60 years old. The majority of cases occur at the age of <60 years due to high outdoor activity[4]. Males are more susceptible to infection due to biological factors, such as the immunosuppressive effect of testosterone and higher outdoor activity [5].


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**Table 1.** Sample Characteristics

| Variable | Dengue Fever (N= 56) % | Dengue Hemorrhagic Fever (N= 44) % | Total % |
|---|---|---|---|
| Age<br>Average ± SD | 51.23 ± 14.85 | 53.52 ± 9.33 | 52.24 ± 12.71 |
| Gender | | | |
| Male | 24 (24) | 28 (28) | 52 (52) |
| Female | 32 (32) | 16 (16) | 48 (48) |

Based on infection status, the majority of respondents had secondary infection status (53%). A total of 56.0% were in the DF (Dengue Fever) category, which is the mildest form of infection. Furthermore, the more severe disease characterized by bleeding showed the highest distribution of Grade 1 DHF (25.0%). Secondary infection is more dominant than primary, especially in endemic areas, due to the phenomenon of antibody-dependent enhancement[1].

**Table 2**. Sample Characteristics Based on Severity of Infection

| Characteristic Severity of Infection | Sample | |
|---|---|---|
| | Frequency | Percentage % |
| DF | 56 | 56 |
| DHF Grade 1 | 25 | 25 |
| DHF Grade 2 | 11 | 11 |
| DHF Grade 3 | 5 | 5 |
| DHF Grade 4 | 3 | 3 |

Analysis of the relationship between variables using the Chi-Square test revealed a significant association between age and the severity of dengue infection (OR = 2.94; 95% CI: 1.25–6.92; p=0.014) .Elderly individuals (>60 years) have a higher risk of severe dengue due to immune system decline caused by immunosenescence, which reduces the activity of T and B cells and slows antibody production[6]. Elevated levels of the ST2 protein in elderly individuals can exacerbate systemic inflammation, contributing to severe complications such as plasma leakage syndrome[7]. Elderly individuals are at higher risk of severe bleeding due to reduced platelet counts and coagulation ability as they age. This condition increases the likelihood of developing severe dengue syndromes, such as dengue hemorrhagic fever or dengue shock syndrome[8]. Additionally, elderly patients tend to have higher viral loads due to decreased ability to control viral replication, worsening the clinical presentation of dengue infection[9].

**Table 3**. Relationship Between Age and Severity of Dengue Virus Infection

| Age | Severity of Dengue Virus Indication | | | | | | p value |
|---|---|---|---|---|---|---|---|
| | DF | | DHF | | Total | | |
| | N | % | N | % | N | % | |
| <60 years | 30 | 53.5 | 34 | 77.2 | 64 | 64 | 0.014 |
| ≥60 years | 26 | 46.4 | 10 | 22.7 | 36 | 36.0 | |


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Chi-square analysis (OR = 2.33; 95% CI: 1.05–5.15; p=0.039) revealed a significant relationship between gender and the severity of dengue infection. Females are more prone to severe dengue due to higher capillary permeability, leading to more severe fluid leakage and an increased risk of dengue shock syndrome[10]. Estrogen in female accelerates dengue virus replication and modulates the immune response, which, despite being rapid, often triggers excessive inflammation[11]. Furthermore, enhanced immune responses in females may result in higher cytokine production, increasing capillary permeability and the risk of severe complications, such as dengue shock syndrome[10,12].

**Table 4.** Relationship Between Gender and Severity of Dengue Virus Infection

| Gender | Severity of Dengue Virus Indication | | | | | | p value |
|---|---|---|---|---|---|---|---|
| | DF | | DHF | | Total | | |
| | N | % | N | % | N | % | |
| Male | 24 | 42.9 | 28 | 63.6 | 52 | 52.0 | 0.039 |
| Female | 32 | 57.1 | 16 | 36.4 | 48 | 48.0 | |

Secondary dengue infection significantly increased the odds of severe dengue compared to primary infection (OR = 5.40; 95% CI: 2.24–13.04; p=0.001). During secondary infection with a different dengue virus serotype, antibodies from the primary infection can enhance viral replication through the Antibody-Dependent Enhancement (ADE) mechanism. This process accelerates viral replication, increases viral load, and triggers excessive inflammatory responses, worsening the patient's condition[13]. Cytokine production, including IL-1, IL-6, and TNF-α, during secondary infection causes endothelial damage, plasma leakage, and severe complications[14].

**Table 5.** Relationship Between Infection Status and Severity of Dengue Virus Infection

| Infection Status | Severity of Dengue Virus Indication | | | | | | p value |
|---|---|---|---|---|---|---|---|
| | DF | | DHF | | Total | | |
| | N | % | N | % | N | % | |
| Primary | 36 | 64.2 | 11 | 25 | 47 | 47.0 | 0.001 |
| Secondary | 20 | 35.7 | 33 | 75 | 53 | 53.0 | |

## Discussion

The observed demographic distribution, with most cases among individuals under 60 years old, might be attributed to their higher outdoor activity levels, which increase exposure to mosquito bites, as noted in two other studies in similar age groups and activity contexts.[10,11] Similarly, the finding that males are more susceptible to infection could be linked to biological factors, such as the immunosuppressive effect of testosterone, and to greater outdoor activity among males than among females.[12]The prevalence of secondary infection status among respondents (53%), especially in endemic areas, aligns with the phenomenon of antibody-dependent enhancement, which increases the likelihood of re-infection with different serotypes.[13,14]

The significant association between age and dengue severity suggests that elderly individuals (>60 years) face a higher risk of severe dengue (p=0.014). This is often explained by immunosenescence, the age-related decline in immune system function, leading to reduced T and B cell activity and slower antibody production. Elevated levels of ST2 protein in the elderly can exacerbate systemic inflammation, contributing to severe complications like plasma leakage syndrome. Furthermore, older adults are


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more prone to severe bleeding due to reduced platelet counts and coagulation ability, increasing the risk of dengue hemorrhagic fever or dengue shock syndrome. Decreased ability to control viral replication in elderly patients can also lead to higher viral loads and a worsening clinical presentation.[15,16]The significant relationship between gender and dengue severity (p=0.039), with female tending to experience more severe outcomes, can be explained by several factors. Female are reported to have higher capillary permeability, which can lead to more severe fluid leakage and an increased risk of dengue shock syndrome[10]. Additionally, estrogen in female has been shown to accelerate dengue virus replication and modulate the immune response, potentially triggering excessive inflammation despite a rapid response[11]. Females' immune systems may produce higher levels of cytokines, further increasing capillary permeability and the risk of severe complications, such as dengue shock syndrome.[17]

Finally, the strong association between secondary dengue infection and an increased risk of severe disease (p=0.001) is well established. During a secondary infection with a different dengue virus serotype, pre-existing antibodies from the primary infection can paradoxically enhance viral replication through the Antibody-Dependent Enhancement (ADE) mechanism.[12,18] This process accelerates viral replication, increases viral load, and triggers an excessive inflammatory response, thereby worsening the patient's condition. This intense immune response can lead to increased cytokine production (e.g., IL-1, IL-6, and TNF-α), causing endothelial damage, plasma leakage, and other severe complications. [19-22]

## Limitations

This study has several limitations. First, the cross-sectional design limits the ability to infer causal relationships between the studied variables and dengue severity. Second, the analysis was based on unadjusted associations, and potential confounding factors were not controlled. Third, this study was conducted in a single center, which may limit the generalizability of the findings to other settings. Lastly, although the sample size met the minimum requirement, the relatively small number of participants may affect the precision of the effect estimates.

## Conclusion

Age, gender, and infection status were significantly associated with dengue severity among adult patients treated at Sanjiwani Gianyar Regional General Hospital in 2023. Patients aged ≥60 years, females, and those with secondary infection showed higher odds of severe dengue. These findings may assist clinicians in identifying patients who require closer monitoring during hospitalization. Further multicenter studies with multivariable analyses are recommended to confirm these associations.

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## Conflict of Interest

All authors declare no conflict of interest, including honorarium, grants, membership, employment, ownership of stock, or any other interest or non-financial interest such as personal or professional relation, affiliation, and knowledge of the research topic.

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