**Investigating The Association Between Clinical and Laboratory Characteristics, Comorbidities, Signs and Symptoms, and the Development of Severe Dengue in Adult Patients in Dhaka City: A Retrospective Study**

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**Abstract**

**Background**: Dengue incidence in Bangladesh has surged, resulting in the deadliest outbreak in 2023 and continued high levels in 2024. Despite aggressive control measures, dengue persists, especially in Dhaka, where there has also been a rise in comorbidities and new symptoms. This study aims to evaluate clinical and laboratory characteristics to understand factors associated with severe dengue.

**Methods**: A retrospective case-control study was conducted on 435 dengue patients admitted to Dhaka Medical College Hospital between July and August 2024. Demographic, clinical, and laboratory data were collected and analyzed using univariate and multivariable logistic regression to identify predictors of disease severity.

**Results**: Of the patients, 60.92% were male, and 53.16% were under 30. Comorbidities like diabetes (AOR 2.79; 95% CI: 1.84–3.15) and hypertension (AOR 2.67; 95% CI: 1.23–5.63) were significantly associated with severe dengue. Symptoms such as abdominal pain (AOR 1.97), vomiting (AOR 1.68), and headache (AOR 1.36) also indicated increased severity. Severe dengue cases had elevated hematocrit, serum creatinine, AST, ALT, pulse rate, and length of stay, while white blood cell count, platelet count, and albumin levels were lower.

**Conclusions**: This study revealed distinct clinical and laboratory differences between severe and non-severe dengue patients. Comorbidities such as diabetes and hypertension, along with symptoms like abdominal pain and vomiting, were key predictors of severe dengue. These findings suggest that patients with these risk factors require closer monitoring to reduce morbidity and mortality. Larger studies are needed to validate these results.

***Keywords: Bangladesh, Case-control Study, Dengue, Retrospective Study, Risk factors, Severe dengue***

**Introduction**

Dengue is a viral illness originated by the dengue virus (DENV), disseminated to humans via the bite of mosquitoes carrying the infection (WHO, 2023a). Dengue fever is prevalent in both urban and semi-urban environments within tropical and subtropical regions, posing a threat to over 50% of the global population (Bhowmik et al., 2023) and is estimated to occur annually in over 100 endemic countries, leads to an estimated annual occurrence of 100–400 million infections worldwide (WHO, 2023a). The prevalence of dengue has surged by a factor of 30 in the past five decades (WHO, 2018). While initial accounts of substantial epidemics resembling a disease potentially identified as dengue emerged on three continents (Asia, Africa, and North America) in 1779 and 1780, there were earlier reports of illnesses displaying clinical compatibility with dengue fever (Gubler, 1998).

During the 1950s, a significant dengue outbreak was documented in Thailand, the Philippines, and Indonesia in the Asian region (Ong et al., 2022; Urcuqui-Inchima et al., 2010). During the late 1970s, dengue had gained widespread prevalence throughout Southeast Asian countries, with Dengue Hemorrhagic Fever (DHF) emerging as a leading factor behind hospitalizations and fatalities, particularly among children in Thailand. Before the year 2004, Thailand consistently documented the highest annual incidence of dengue cases within Southeast Asia, averaging nearly 69,000 reported cases each year between 1985 and 1999 (Limkittikul et al., 2014). After 2004, Indonesia assumed the foremost position in reporting dengue cases in the region, contributing 57% of the cases reported to the WHO Southeast Asia region in 2006 (WHO, 2007). By 2019, the Philippines recorded an unprecedented 437,563 cases, representing the highest number of dengue cases ever documented globally (Ong et al., 2022). Overall, in 2023 globally, 6.5 million cases and >6800 deaths attributed to DENV were recorded, marking a historic milestone. Two distinct hotspots of dengue virus circulation emerged: the South American and the South and Southeast Asian regions (Haider et al., 2024).

As East Pakistan, Bangladesh experienced its initial dengue outbreak in 1964, coinciding with the introduction of the term "Dacca fever." In recent years, Bangladesh has been notably affected by dengue viruses and stands among the nation’s most significantly impacted (Sharmin et al., 2015). Official government monitoring systems have documented fatalities corresponding to significant outbreaks. In 2019, Bangladesh faced a widespread dengue epidemic, with 101,354 recorded cases and 164 deaths attributed to dengue (Ullah et al., 2024). The peak of cases and fatalities occurred predominantly during the summer and autumn months. The geographical distribution of cases reported in 2019 encompassed all districts of the country, with a higher frequency observed. This pattern disproportionately affected males and predominantly impacted individuals in the younger age groups (DGHS, 2019).

The Ministry of Health & Family Welfare in Bangladesh has officially reported 34,438 laboratory-confirmed dengue cases and 27 associated deaths from January 1 to October 4, 2024. From the initial decade (2000–2010) to the subsequent one (2011–2022), there has been an 8.3-fold surge in dengue cases, coupled with a 2.2-fold rise in annual fatalities in Bangladesh (Hasan et al., 2024). While Dhaka, historically the most severely affected division, has experienced a high number of cases, has seen the highest number of cases ever recorded outside Dhaka, comprising 64.82% (n=193,216) of the total cases. Dhaka still has a notable number of dengue-related deaths, with 638 reported and a case fatality rate of 0.8%, compared to 0.3% outside Dhaka (DGHS, 2023; Haider, Asaduzzaman, et al., 2023; Islam, Hemo, et al., 2023). The country has been marked by unusually high temperatures, intolerable humidity, irregular rainfall, and a significant prevalence of dengue cases, contributing to an increase in mosquito populations nationwide (Haider, Hasan, et al., 2023; Islam, Hasan, et al., 2023).

Emphasizing the severity of the current epidemic is imperative. Regrettably, the authorities appear to be addressing the situation with inadequate attention, as reflected not only in significant underreporting but also in the lack of comprehensive public health awareness efforts directed at both the general populace and healthcare practitioners. It is imperative to urgently initiate such campaigns, with a specific focus on early and consistent diagnosis of dengue infections and the provision of supportive clinical management. These measures have demonstrated considerable efficacy in substantially decreasing mortality rates associated with this highly contagious disease (Kala et al., 2023; Pilot et al., 2019).

Conversely, ensuring prompt access to appropriate care for dengue patients through primary healthcare providers can lower fatality rates to approximately 1% while also minimizing unnecessary hospitalizations (Yeh et al., 2017). Identifying patients transitioning from mild to severe disease can be challenging, but it is a serious concern since proper care can prevent the development of more severe clinical conditions (WHO, 2023a). Nevertheless, there is a paucity of literature delving into the interplay between demographic profiles, clinical features, comorbidities, and the prognosis/complications of dengue in Bangladesh. Grasping this relationship holds paramount importance in pinpointing high-risk dengue patients. The utilization of diverse warning indicators can play a pivotal role in promptly identifying potentially severe cases, facilitating timely treatment, averting unnecessary hospitalizations, and mitigating the case fatality rate of the disease. However, numerous clinical and epidemiological facets, particularly within the context of Bangladesh, remain inadequately elucidated. Hence, the primary aim of this study is to investigate the association between various clinical characteristics, comorbidities, signs and symptoms with severe cases of dengue.

**Methods**

We adhered to the STROBE guideline for reporting case-control studies in epidemiology (Table S1) (Cuschieri, 2019).

**Data source**

Trained interviewers (medical assistants) conducted interviews with both cases and controls over a two-month period, from January 1 to August 31, 2024, at Dhaka Medical College Hospital (DMCH) in Dhaka, Bangladesh. The ninth floor of DMCH features a dedicated section for the treatment and care of dengue patients. Hospital electronic medical records were used to extract administrative, laboratory, microbiological, and radiological data. Medically trained research assistants performed the data extraction, which was followed by rule-based validation for the entire dataset. Additionally, 10% of the cases were randomly selected for repeat data entry by another research assistant, and any discrepancies were addressed through an independent review of medical case notes by one of the authors. The extracted data was de-identified for analysis. A pretested and standardized questionnaire was utilized, and all clinical records were reviewed by doctors.

**Sampling design and sample size**

We determined the sample size by utilizing an online sample size calculator (Sampsize, 2023). In conducting this case-control study, we took into account parameters including 80% power, a 95% confidence level, a 7% exposure rate among controls, an odds ratio (OR) of 2.5, and a 1:2 allocation ratio for each group. The computation revealed a requirement for 435 participants, with 145 designated as cases and 290 as controls. We determined the percentage for exposed controls based on previous research by Badawi et al. In their study, chance ratios for severe dengue in patients with comorbidities such as diabetes, hypertension, and heart disease ranged from 2 to 4. Considering this, we chose an odds ratio of 2.0 (Badawi et al., 2018).

**Inclusion exclusion criteria**

This research enrolls participants aged 18 years and above who have been diagnosed with severe dengue as per the 2009 Dengue Classification outlined by the World Health Organization (WHO, 2023a). To ensure clarity, it's important to note that all severe dengue cases in our study underwent treatment in the intensive care unit at designated research sites. The control group comprises adults aged 18 years and older diagnosed with non-severe dengue, who did not advance to severe dengue during their hospital stay. Individuals with non-severe dengue in the control group receive treatment in a specified general medical ward at our research site. Pregnant patients with dengue will be excluded from the study.

**Variables**

***Outcome variables:***

To construct our outcome variable indicating severity level, patients were designated as 1 for severe cases or otherwise recorded as 0 for non-severe cases. Clinical data was derived from the hematology/biochemical test reports of the patients, and a thorough review of all records was conducted by medical specialists.

***Independent variables:***

Numerous potential risk factors associated with severe dengue have been explored, encompassing demographic details such as age, gender, marital status, education level, and monthly income. Additionally, pre-existing medical conditions including obesity, diabetes, hypertension, chronic pulmonary disease, and ischemic heart disease were investigated. The study also considered presenting signs and symptoms upon admission, such as abdominal pain, diarrhea, vomiting, lethargy, headache, rash, chills or rigors, nausea, hemorrhagic symptoms, and musculoskeletal pain. According to the WHO Guidelines, obesity was defined as having a body mass index (BMI) of 27.5 kg/m2 or higher, based on admission data (WHO, 2023b).

**Statistical Analysis**

To examine the relationship between severe dengue and its associated risk factors, we conducted bivariate analyses, employing methods such as the chi-square test and univariate [unadjusted] logistic regression models. We used all potential covariates in univariate models. We used an arbitrary p—value of ≤ 0.20 as a criterion to include covariates in the multivariable models (Hasan et al., 2020) . We used stepwise procedures to select the best model. Therefore, in our final model, we had included all significant covariates and some key variables related to the outcome. In univariate analyses, each variable is individually incorporated into the logistic regression model, presenting a crude odds ratio (COR). The multivariable logistic regression model was utilized to present an adjusted odds ratio (AOR), accounting for multiple variables simultaneously.

**Variable Selection**

To assess multicollinearity in the final model, we employed a cut-off value of 4.00 for the variance inflation factor (VIF), following the methodology outlined by (Hasan et al., 2023; Kim, 2019). All variables were included in this stage of the model, as each variable's VIF value was below 4.00.

**Model evaluation**

To evaluate the precision of the optimal model, we employed several metrics, including the Area under the Receiver Operating Characteristic (AUROC) and the Hosmer-Lemeshow goodness-of-fit test. Enhanced model performance is reflected by higher AUROC values. Within the ROC curve, a reduced P-value signifies the model's effective discrimination between two categories, with an area under the curve surpassing 0.50 indicative of superior discrimination (Wu et al., 2021). The Hosmer-Lemeshow goodness-of-fit test evaluates the similarity between model-estimated probabilities and observed outcomes. Typically assessed through a goodness-of-fit test, a Hosmer-Lemeshow test yielding a P-value above 0.05 indicates the model's effectiveness in precisely categorizing observations into outcome categories (Hasan et al., 2022).

**Results**

This study comprised 145 cases and 290 controls who were hospitalized at DMCH, our study site, between January 1 to August 31, 2024. In this case-control study with a case-to-control ratio of 1:2, the cases included 75 (51.72%) males and 70 (48.28%) females, while the control group consisted of 190 (65.5%) males and 100 (34.5%) females. Regarding age, 60 (43.48%) cases were in the 0-29 years category, and 78 (56.52%) were greater than 29 years. In the cases group, 85 (59.44%) were married, and 58 (40.56%) were unmarried. Significant associations were observed between cases and controls concerning age, gender, and marital status (p<0.05). No discernible differences were found in dengue severity with respect to education level and monthly income (p>0.05). However, a small portion of the cases had higher secondary and above education (4.96%), while the majority had primary education (41.13%) **(Table 1)**.

The study compared five comorbidities, namely obesity, diabetes, hypertension, chronic pulmonary illnesses, and ischemic heart disease. Diabetes, chronic pulmonary disease, and ischemic heart disease were notably more prevalent among cases than controls (p<0.05). In the cases group, 11 (7.59%), 23 (15.86%), and 14 (9.66%) patients had diabetes, chronic pulmonary disease, and ischemic heart disease, respectively. Additionally, symptoms such as abdominal pain, diarrhea, vomiting, and lethargy were significantly associated with severe dengue patients (p<0.05). In the cases group, 84 (58.3%), 33 (22.80%), 14 (9.66%), 28 (19.44%), and 27 (18.62%) patients exhibited abdominal pain, diarrhea, vomiting, lethargy, and nausea symptoms, respectively **(Table 1)**.

The median values for age (Median=32), hematocrit (49.62), serum creatinine (132.11), AST (171.13), ALT (123.17), pulse rate (89.68), temperature (38.68), and length of hospital stay (5.12) were significantly higher in the cases compared to the controls. In contrast, white blood cell count (4.90), platelet count (85.54), total bilirubin (10.34), total protein (62.74), albumin (39.78), and globulin levels (24.72) were significantly lower in the cases than in the controls **(Table 2).**

**Table 3** presents information on the Crude Odds Ratio (COR) and Adjusted Odds Ratio (AOR) for the association between various factors and dengue severity. Results indicate that patients older than 29 years were more likely to experience severe dengue (COR: 1.82; 95% CI: 1.20-2.78), and after adjusting the model, this likelihood remained (AOR: 1.34; 95% CI: 1.12-4.72) compared to patients aged 29 years or younger. Female patients (COR: 1.77; 95% CI: 1.18-2.66) and married patients (COR: 2.04; 95% CI: 1.36-3.08) were also more likely to have severe dengue in the unadjusted model, but these associations became insignificant in the adjusted model.

The univariate logistic regression analysis revealed a statistically significant association between severe dengue and diabetes. Severe cases exhibited 1.62 times higher odds (COR: 1.62; 95% CI: 1.10-3.65) in the unadjusted model and 2.79 times higher odds (AOR: 2.79; 95% CI: 1.84-3.15) in the adjusted model compared to individuals without diabetes. Similarly, severe dengue cases had 2.19 times higher odds (COR: 2.19; 95% CI: 1.18-4.07) and 1.61 times higher odds (COR: 1.61; 95% CI: 1.17-3.34) in the unadjusted model for chronic pulmonary disease and ischemic heart disease, respectively. However, these associations were not significant in the adjusted model.

Comparing different clinical signs and symptoms between cases and controls, univariate and multivariable analyses identified abdominal pain as a higher odds and significant predictor of severe dengue (COR: 2.39; 95% CI: 1.60-3.61 and AOR: 1.97; 95% CI: 1.15-2.85). Although diarrhea and nausea were significant predictors in the crude model (COR: 1.41; 95% CI: 1.18-1.78 and COR: 2.06; 95% CI: 1.16-3.64, respectively), they became insignificant in the adjusted model. Vomiting and lethargy remained significant in both crude and adjusted models. In the adjusted model, severe dengue cases had higher odds of 1.68 (COR: 1.68; 95% CI: 1.03-2.19) and 1.55 (COR: 1.55; 95% CI: 1.01-2.22) for vomiting and lethargy, respectively, compared to their counterparts. Additionally, severe dengue cases had 1.36 times higher odds (COR: 1.36; 95% CI: 1.14-2.65) in the adjusted model than individuals without headache.

As per the Variance Inflation Factor (VIF) analysis, all variables exhibit values less than 5, indicating the absence of multicollinearity in the dataset. Moreover, the AUC value of 72.46% in **Table 4** suggests that the classification accuracy is deemed acceptable (**Figure 1)**. Additionally, the model successfully passed the Hosmer and Lemeshow goodness-of-fit test (value = 10.46, degrees of freedom = 8, P-value = 0.234), signifying no lack of fit in the model.

**Discussion:**

This study evaluated the risk factors associated with severe dengue among 145 cases and 290 controls hospitalized during the 2024 dengue outbreak in Bangladesh. Our study aimed to identify risk factors for severe dengue during this outbreak, revealing a complex interplay of demographic characteristics, comorbidities, and symptoms. The findings underscore the significance of demographic factors, comorbidities, and clinical symptoms in predicting the severity of dengue, aligning with prior studies while offering fresh insights into the Bangladesh-specific context.

A significant relationship between age and dengue severity was observed, with individuals aged over 29 years being more susceptible to severe outcomes. This finding is consistent with previous research highlighting the vulnerability of older populations to severe dengue complications. The physiological changes with aging, such as weakened immune responses, may partly explain this increased risk (Huang et al., 2023; Lin et al., 2017). Interestingly, while more males were affected in both cases and controls, females showed higher odds of severe dengue in the unadjusted analysis, which consistent with earlier literature that men are more susceptible to dengue infection during outbreaks, while women are more associated with severe cases in Bangladesh (Hossain et al., 2023; Islam et al., n.d.; Sami et al., 2023) and other countries (Sangkaew et al., 2021; Srisuphanunt et al., 2022). Sex-specific discrepancies may be linked to differences in healthcare-seeking behavior, visitation patterns, and types of care. However, this effect became non-significant after adjusting for other factors, suggesting that while gender may influence dengue infection rates, it does not independently predict severity.

Our study reinforced the established role of comorbid conditions such as diabetes, chronic pulmonary disease, and ischemic heart disease in escalating the risk of severe dengue. Particularly, diabetes emerged as a strong predictor of severe outcomes, with an adjusted odds ratio of 2.79. This aligns with global studies that emphasize diabetes as a critical risk factor due to its impact on immune modulation and endothelial dysfunction, which can exacerbate the complications associated with dengue (dos Santos et al., 2024; Latt et al., 2020; Lee et al., 2020; Ng et al., 2022; Toledo et al., 2016) and previous studies in Bangladesh (Bhowmik et al., 2023; Hossain et al., 2023). Chronic pulmonary disease and ischemic heart disease, while significant in univariate analysis, did not retain their independent predictive power in multivariate analysis. This highlights the need for more nuanced research into the specific mechanisms by which these conditions interact with dengue pathophysiology.

Abdominal pain, vomiting, and lethargy were significantly associated with severe dengue in both crude and adjusted models. These symptoms have long been recognized as warning signs for progression to severe dengue Abdominal pain showed a strong association with severe outcomes, which is consistent with previous findings suggesting that it is a marker of plasma leakage and impending shock​ (Akram et al., 2023; Al-Araimi et al., 2011; Gupta et al., 2017; Islam et al., 2022; Sami et al., 2023). Conversely, the presence of headache was associated with lower odds of severe dengue, which is an intriguing finding corroborated by recent studies suggesting that headache may inversely correlate with disease severity​. In a retrospective cohort study conducted in Singapore, involving 82 patients with dengue hemorrhagic fever (DHF) and 1855 patients with dengue fever (DF), it was reported that the presence of headache upon presentation was linked to reduced odds of developing DHF (Ng et al., 2022).

The acceptable classification accuracy of 72.46% and the passing of the Hosmer-Lemeshow test suggest that our model is robust in identifying the predictors of severe dengue. The absence of multicollinearity further supports the reliability of these findings. However, while the model performs well in classifying patients, it leaves room for improvement, particularly in accounting for factors beyond demographic and clinical parameters, such as vector exposure and environmental conditions in present outbreak​.

The results of this study highlight the importance of targeted public health interventions, especially for older adults and individuals with comorbidities. Tailored dengue awareness and prevention campaigns that emphasize the risk of severe outcomes in these populations are crucial. Additionally, healthcare systems should ensure prompt and aggressive management of patients presenting with warning signs like abdominal pain and vomiting to mitigate the risk of severe dengue complications. Gender differences in healthcare access and outcomes, as highlighted by the excess severe cases among females, also warrant further exploration to address potential disparities in care delivery.

Beyond the current significance, this study limited by conducting at a single site, which may lack the generalizability of the findings. Additionally, due to the retrospective design, we were reliant on existing records, which may not have captured all relevant risk factors or comorbid conditions. Future studies should aim to include multiple centers and prospective designs to confirm these findings and explore additional risk factors for severe dengue.

**Conclusion**

In summary, our comprehensive case-control investigation underscores the significance of integrating socio-economic variables such as age, gender, and marital status, as well as comorbidities like diabetes and chronic pulmonary disease, along with key signs and symptoms such as abdominal pain, diarrhea, vomiting, and lethargy, in assessing the severity of dengue cases. This research contributes novel insights to the identification of crucial risk factors associated with severe dengue, enhancing our understanding of early detection and treatment. Future studies should delve deeper into the progression from non-severe to severe dengue, building upon the findings of this research.

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**Tables and Figures**

**Table 1: Chi-square test of the socio-demographic characteristics, comorbidities, and signs and symptoms distribution among both cases and controls**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure variables** | **Cases**  **n (%)** | **Controls**  **n (%)** | **Totals**  **n (%)** | **p-value** |
| **Socio-demographic** |  |  |  |  |
| **Age** |  |  |  |  |
| ≤ 29 years | 60 (43.48) | 150 (58.37) | 210 (53.16) | **0.005** |
| > 29 years | 78 (56.52) | 107 (41.63) | 185 (46.84) |  |
| **Gender** |  |  |  |  |
| Male | 75 (51.72) | 190 (65.5) | 265 (60.92) | **0.006** |
| Female | 70 (48.28) | 100 (34.5) | 170 (39.08) |  |
| **Marital Status** |  |  |  |  |
| Married | 85 (59.44) | 120 (41.81) | 205 (47.67) | **<0.001** |
| Unmarried | 58 (40.56) | 167 (58 .19) | 225 (52.33) |  |
| **Education level** |  |  |  |  |
| Higher Secondary or above | 7 (4.96) | 7 (2.46) | 14 (3.29) | 0.316 |
| Secondary | 27 (19.15) | 50 (17.61) | 77 (18.12) |  |
| Primary | 58 (41.13) | 107 (37.68) | 165 (38.82) |  |
| No education | 49 (34.75) | 120 (42.25) | 169 (39.76) |  |
| **Monthly Income** |  |  |  |  |
| Low | 78 (56.52) | 140 (48.95) | 218 (51.42) | **0.143** |
| Medium | 27 (19.57) | 81 (28.32) | 108 (25.47) |  |
| High | 33 (23.91) | 65 (22.73) | 98 (23.11) |  |
| **Comorbidities** |  |  |  |  |
| **Obesity** |  |  |  |  |
| Yes | 55 (37.93) | 107 (36.90) | 162 (37.24) | 0.833 |
| No | 90 (62.07) | 183 (63.10) | 273 (62.76) |  |
| **Diabetes** |  |  |  |  |
| Yes | 11 (7.59) | 14 (4.83) | 25 (94.25) | **0.044** |
| No | 134 (92.41) | 276 (95.17) | 410 (5.75) |  |
| **Hypertension** |  |  |  |  |
| Yes | 19 (13.10) | 28 (9.66) | 47 (10.80) | 0.275 |
| No | 126 (86.90) | 262 (90.34) | 388 (89.20) |  |
| **Chronic Pulmonary Disease** |  |  |  |  |
| Yes | 23 (15.86) | 23 (7.93) | 46 (10.57) | **0.011** |
| No | 122 (84.14) | 267 (92.07) | 389 (89.43) |  |
| **Ischemic Heart Disease** |  |  |  |  |
| Yes | 14 (9.66) | 18 (6.21) | 32 (7.36) | **0.197** |
| No | 131 (90.34) | 272 (93.79) | 403 (92.64) |  |
| **Signs and symptoms** |  |  |  |  |
| **Abdominal Pain** |  |  |  |  |
| Yes | 84 (58.3) | 107 (36.9) | 191 (44.01) | **<0.001** |
| No | 60 (41.7) | 183 (63.1) | 243 (55.99) |  |
| **Diarrhea** |  |  |  |  |
| Yes | 33 (22.8) | 61 (21.03) | 94 (21.61) | **<0.001** |
| No | 112 (77.2) | 229 (78.97) | 341 (78.39) |  |
| **Vomiting** |  |  |  |  |
| Yes | 14 (9.66) | 22 (7.58) | 36 (8.28) | **0.004** |
| No | 131 (90.34) | 268 (92.41) | 399 (91.72) |  |
| **Lethargy** |  |  |  |  |
| Yes | 28 (19.44) | 21 (7.27) | 49 (11.32) | **<0.001** |
| No | 116 (80.56) | 268 (92.73) | 384 (88.68) |  |
| **Headache** |  |  |  |  |
| Yes | 110 (76.39) | 225 (77.59) | 335 (77.19) | 0.742 |
| No | 34 (23.61) | 65 (22.41) | 99 (22.81) |  |
| **Rash** |  |  |  |  |
| Yes | 103 (71.53) | 203 (70.00) | 306 (70.51) | 0.461 |
| No | 41 (28.47) | 87 (30.00) | 128 (29.49) |  |
| **Chills and Rigors** |  |  |  |  |
| Yes | 39 (26.90) | 79 (27.24) | 118 (27.13) | 0.939 |
| No | 106 (73.10) | 211 (72.75) | 317 (72.87) |  |
| **Nausea** |  |  |  |  |
| Yes | 27 (18.62) | 29 (10.00) | 56 (12.87) | **0.011** |
| No | 118 (81.38) | 261 (90.00) | 379 (87.13) |  |
| **Hemorrhagic** |  |  |  |  |
| Yes | 108 (75.0) | 207 (71.38) | 412 (95.37) | 0.854 |
| No | 36 (25.0) | 83 (28.62) | 20 (4.63) |  |
| **Musculoskeletal Pain** |  |  |  |  |
| Yes | 108 (75.0) | 207 (71.38) | 315 (72.58) | 0.426 |
| No | 36 (25.0) | 83 (28.62) | 119 (27.42) |  |
| **Total** | 145 (33.33) | 290 (66.67) | 435 (100.00) |  |

**Table 2: Comparison of Laboratory Factors in Severe vs. Non-Severe Dengue Patients**

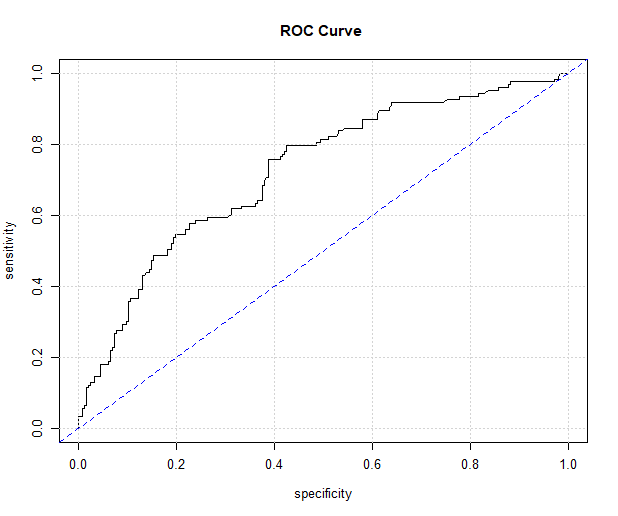
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Cases**  **Median (IQR)** | **Controls**  **Median (IQR)** | **Totals**  **Median (IQR)** | **p-value** |
| **Age (Years)** | 32 (22) | 25 (15) | 27 (19) | <0.001 |
| **WBCs (cells × 109 /L)** | 4.90 (2.37) | 5.51 (3.50) | 5.20 (3.12) | <0.001 |
| **Thrombocytes (cells × 109 /L)** | 85.54 (17.15) | 94.49 (15.72) | 91.55 (14.20) | <0.001 |
| **Hematocrit (%)** | 49.62 (5.67) | 39.80 (4.96) | 42.46 (8.53) | <0.001 |
| **Hemoglobin (g/dL)** | 15.36 (5.27) | 15.19 (4.77) | 15.23 (4.78) | 0.264 |
| **Serum Creatinine (μmol/L)** | 132.11 (29.51) | 104.80 (14.54) | 111.01 (18.21) | <0.001 |
| **Total bilirubin (μmol/L)** | 10.34 (2.23) | 12.46 (2.36) | 11.80 (2.5) | <0.001 |
| **AST (IU/L)** | 171.13 (62.03) | 127.76 (48.65) | 142.53 (54.43) | <0.001 |
| **ALT (IU/L)** | 123.17 (25.39) | 114.32 (25.12) | 117.44 (25.03) | <0.001 |
| **Total protein (g/L)** | 62.74 (2.40) | 65.01 (5.13) | 63.67 (4.58) | <0.001 |
| **Albumin (g/L)** | 39.78 (4.14) | 42.36 (2.73) | 41.72 (3.07) | <0.001 |
| **Globulin (g/L)** | 24.72 (4.96) | 27.53 (2.63) | 26.94 (3.05) | <0.001 |
| **Pulse rate (BPM)** | 89.68 (4.15) | 88.14 (4.56) | 88.58 (4.49) | <0.001 |
| **Temperature (◦C)** | 38.68 (1.52) | 37.99 (1.03) | 38.14 (1.19) | <0.001 |
| **Hospitalization length (days)** | 5.12 (0.98) | 3.03 (0.98) | 3.52 (1.74) | <0.001 |

**Table 3: The association between socio-demographic characteristics, comorbidities, and the distribution of signs and symptoms among both cases and controls using univariate and multivariable models**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure variables** | **COR (95% CI)** | **P-value** | **AOR (95% CI)** | **P-value** |
| **Socio-demographic** |  |  |  |  |
| **Age** |  |  |  |  |
| > 29 years | 1.82 (1.20-2.78) | **0.005** | 1.34 (1.12-4.72) | **0.028** |
| ≤ 29 years | Reference |  | Reference |  |
| **Gender** |  |  |  |  |
| Female | 1.77 (1.18-2.66) | **0.006** | 1.70 (1.42-2.17) | 0.071 |
| Male | Reference |  | Reference |  |
| **Marital Status** |  |  |  |  |
| Married | 2.04 (1.36-3.08) | **<0.001** | 1.49 (1.10-3.14) | 0.296 |
| Unmarried | Reference |  | Reference |  |
| **Highest Education** |  |  |  |  |
| Higher Secondary or above | 2.45 (0.80-7.51) | **0.110** | 4.42 (0.93-8.22) | 0.086 |
| Secondary | 1.32 (0.74-2.34) | 0.340 | 1.92 (0.45-3.11) | 0.108 |
| Primary | 1.33 (0.84-2.11) | 0.228 | 1.56 (0.78-2.98) | 0.112 |
| No education | Reference |  | Reference |  |
| **Monthly Income** |  |  |  |  |
| Low | 1.10 (0.67-1.83) | 0.717 | 1.23 (0.66-2.32) | 0.523 |
| Medium | 0.66 (0.36-1.20) | **0.172** | 0.92 (0.46-1.87) | 0.824 |
| High | Reference |  | Reference |  |
| **Comorbidities** |  |  |  |  |
| **Obesity** |  |  |  |  |
| Yes | 1.05 (0.69-1.57) | 0.833 | 1.35 (0.79-2.26) | 0.232 |
| No | Reference |  |  |  |
| **Diabetics** |  |  |  |  |
| Yes | 1.62 (1.10-3.65) | **0.044** | 2.79 (1.84-3.15) | **0.034** |
| No | Reference |  |  |  |
| **Hypertension** |  |  |  |  |
| Yes | 1.41 (0.75-2.61) | 0.275 | 2.67 (1.23-5.63) | **0.037** |
| No | Reference |  |  |  |
| **Chronic Pulmonary Disease** |  |  |  |  |
| Yes | 2.19 (1.18-4.07) | **0.011** | 1.64 (0.47-3.98) | 0.632 |
| No | Reference |  |  |  |
| **Ischemic Heart Disease** |  |  |  |  |
| Yes | 1.61 (1.17-3.34) | 0.019 | 1.51 (0.71-3.18) | 0.279 |
| No | Reference |  |  |  |
| **Signs and Symptoms** |  |  |  |  |
| **Abdominal Pain** |  |  |  |  |
| Yes | 2.39 (1.60-3.61) | **<0.001** | 1.97 (1.15-2.85) | **<0.001** |
| No | Reference |  |  |  |
| **Diarrhea** |  |  |  |  |
| Yes | 1.41 (1.18-1.78) | **<0.001** | 0.97 (0.84-1.31) | 0.193 |
| No | Reference |  |  |  |
| **Vomiting** |  |  |  |  |
| Yes | 1.50 (1.23-2.60) | **0.004** | 1.68 (1.03-2.19) | **0.031** |
| No | Reference |  |  |  |
| **Lethargy** |  |  |  |  |
| Yes | 3.08 (1.69-5.71) | **<0.001** | 1.55 (1.01-2.22) | **0.022** |
| No | Reference |  |  |  |
| **Headache** |  |  |  |  |
| Yes | 1.93 (0.59-2.51) | 0.742 | 1.36 (1.14-2.65) | **<0.001** |
| No | Reference |  |  |  |
| **Rash** |  |  |  |  |
| Yes | 1.08 (0.70-1.68) | 0.461 | 1.68 (1.13-1.91) | **0.013** |
| No | Reference |  |  |  |
| **Chills and Rigors** |  |  |  |  |
| Yes | 0.98 (0.62-1.53) | 0.939 | 1.56 (0.67-1.98) | 0.113 |
| No | Reference |  |  |  |
| **Nausea** |  |  |  |  |
| Yes | 2.06 (1.16-3.64) | **0.011** | 1.68 (0.99-2.99) | 0.204 |
| No | Reference |  |  |  |
| **Hemorrhagic** |  |  |  |  |
| Yes | 1.09 (0.40-2.73) | 0.854 | 1.58 (0.59-1.94) | 0.389 |
| No | Reference |  |  |  |
| **Musculoskeletal Pain** |  |  |  |  |
| Yes | 1.20 (0.77-1.91) | 0.426 | 1.13 (0.65-1.75) | 0.489 |
| No | Reference |  |  |  |

**Table 4: Evaluation of Goodness of Fit and Predictive Accuracy in the Final Model**

|  |  |  |
| --- | --- | --- |
| **Hosmer and Lemeshow’s Goodness of Fit Test:** | | |
| X-squared | Degrees of freedom | P-value |
| 10.46 | 8 | 0.234 |
| **Area Under the Receiver Operating Characteristic Curve (ROC):** | | |
| Value | 72.46% | |



**Figure 1: Goodness of fit and accuracy of the final model**