**Spreading out of Severe Dengue: Signs-Symptoms, Clinical Characteristics, and Comorbidities in Dhaka City**

**Abstract**

**Background**: Dengue incidence in Bangladesh has spread, resulting in the deadliest outbreak in 2023 and continued high levels in 2024. Despite aggressive control measures, dengue persists, especially in Dhaka city, where there has also been a rise in comorbidities and new symptoms. Laboratory and clinical characteristics are evaluated to detect severe dengue infections early and treat the illness effectively, particularly in areas where transmission is prevalent.

**Methods**: A corresponding retrospective case-control study was conducted on 435 dengue patients admitted to different medical college hospitals in Dhaka between January and June 2024. Univariate and multivariable logistic regression was conducted to identify predictors of disease severity using demographic and clinical dengue data.

**Results**: Among 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**: Significant clinical and biochemical differences between patients with severe and non-severe dengue were found in this investigation. Severe dengue was significantly predicted by comorbid conditions including diabetes and hypertension as well as symptoms like vomiting and stomach discomfort. 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:* Case-control, Dengue, Retrospective Study, Severe dengue, Bangladesh,**

**Introduction**

Humans contract dengue, a virus spread by the dengue virus (DENV), when bitten by an infected mosquito [1]. Dengue fever is prevalent in urban and semi-urban environments within tropical and subtropical regions, posing a threat to over 50% of the global population [2]. The estimated cases will cross 100 million in over 100 endemic countries each year [3]. Earlier reports described illnesses exhibiting clinical features consistent with dengue fever [4]. Across the 1950s, there was a notable dengue outbreak across Asia, especially in Thailand, the Philippines, and Indonesia. These outbreaks marked one of the earliest large-scale recognitions of dengue as a major public health concern in Asia, with severe cases presenting as dengue hemorrhagic fever (DHF). This emergence highlighted the disease's growing impact, particularly in tropical and subtropical areas where the Aedes mosquito vectors thrive [5, 6]. Dengue has gained widespread prevalence throughout Southeast Asian countries [7]. The two primary dengue virus circulation hotspots in 2023 are South America and South and Southeast Asia [9]. In 2023, DENV was responsible for around 6800 deaths and 6.5 million cases worldwide, a record high [9]. Bangladesh's Ministry of Health & Family Welfare recorded 34,438 laboratory-confirmed dengue cases between January 1 and October 4, 2024 (https://www.iedcr.gov.bd/). Dengue cases have increased 8.3 times and yearly deaths have increased 2.2 times in Bangladesh over the two decades. (Haider et al., 2024). Dengue kills a disproportionately high number of people in Dhaka, with a case fatality rate of 0.8% compared to 0.3% outside the city [13-15]. Recurrent outbreaks of dengue occurred in recent decades in Dhaka due to rapid urbanization, inadequate waste management, and favorable climatic conditions for the proliferation of **Aedes aegypti** mosquitoes, the primary vector of the disease (Sharmin et al., 2015).

Unusually high temperatures, unbearable humidity, erratic rainfall, and a high incidence of dengue illnesses have all contributed to the nation's rising mosquito populations. Unusually high temperatures, oppressive humidity, erratic rainfall patterns, and a surge in dengue cases have collectively fueled the growth of mosquito populations across the nation [16, 17]. There is a paucity of literature delving into the interplay between demographic profiles, clinical features, comorbidities, and the prognosis/complications of dengue in Bangladesh. The clinical presentation of severe dengue extends beyond the typical symptoms of high fever, rash, and joint pain seen in classical dengue fever. Severe cases are characterized by plasma leakage, severe bleeding, and organ dysfunction, leading to high morbidity and mortality rates if untreated (World Health Organization [WHO], 2009). Additionally, comorbidities such as diabetes, hypertension, and obesity have been identified as potential risk factors that exacerbate the severity of dengue infections (Ming et al., 2020). There was a severe dengue outbreak in Bangladesh in 2024; 101,354 cases were reported, and 164 people died from the disease [11]. The summer and fall seasons saw the highest number of illnesses and fatalities. Although a higher frequency was seen, the geographic distribution of cases recorded in 202419 comprised all of the nation's districts. Males were disproportionately affected by this tendency, which primarily affected younger people [12].

Emphasizing the severity of the current epidemic is imperative. Unfortunately, it seems that the authorities are not paying enough attention to the difficulty. This was evidenced by the absence of extensive public health awareness campaigns. It is imperative to urgently initiate campaigns, with a specific focus on early detection and the provision of supportive clinical management. Consistent diagnoses of dengue infections and campaigns can be considered efficacy in substantially decreasing mortality rates [18].

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 19. 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 3. It suggests that only by analyzing and understanding environmental, biological, or other factors influencing dengue severity healthcare providers accurately assess which patients are more vulnerable to severe outcomes. 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.

**Materials and Methods**

The study adhered to the STROBE guideline for reporting case-control studies in epidemiology (Table S1) 20.

**Study Population**

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 Organization3. The control group comprises adults aged 18 years and older diagnosed with non-severe dengue, who did not advance to severe dengue during the specified general medical ward at the research site. Pregnant patients with dengue were excluded from this study.

Trained interviewers (medical assistants) conducted interviews with both cases and controls over six months, from January 1 to June 30, 2024, from several medical institutions dedicated to providing healthcare support to Dengue patients in Dhaka, Bangladesh. Hospital electronic medical records were used to extract administrative, laboratory, microbiological, and radiological data. Medically trained research assistants performed data extraction, 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 doctors reviewed all clinical records.

**Sampling design and sample size**

In conducting this case-control study, we considered 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. The percentage for exposed controls is based on previous research22. 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, odds ratio of 2.0 has been chosen. Data extractions were continued till getting enough cases and control to meet the ratio.

***Outcome Variable: Dengue severity***

Patients were recorded as for non-severe instances and for severe cases in order to create an outcome variable that indicated severity degree. Clinical data was derived from medical specialists conducted a thorough review of all records the patients' hematology test reports, and medical specialists thoroughly reviewed all records. According to the WHO Guidelines, obesity of dengue the patients was defined as having a body mass index (BMI) of 27.5 kg/m2 or higher, based on admission data 23.

**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  ≤ 0.20) as a criterion to include covariates in the multivariable models24. To choose the best model, we followed stepwise procedures. As a result, all significant covariates as well as a few important outcome-related factors were included in our final model. 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.

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 16,25. All variables were included in this stage of the model, as each variable's VIF value was below 4.00.A number of metrics, such as the Area under the Receiver Operating Characteristic (AUROC) and the Hosmer-Lameshow goodness-of-fit test, to assess the accuracy of the ideal model was used. Enhanced model performance is reflected by higher AUROC values 26. 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 27.

**Results**

This study comprised 145 cases and 290 controls who were hospitalized at DMCH, our study site, between January 1 to June 30, 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 concerning 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%)presented in Table 1.

Five comorbidities-obesity, diabetes, hypertension, chronic pulmonary diseases, and ischemic heart disease were compared in the study. Cases were much more likely than controls to have diabetes, ischaemic heart disease, and chronic pulmonary illness (p<0.05). Diabetes, chronic pulmonary disease, and ischaemic heart disease were present in 11 (7.59%), 23 (15.86%), and 14 (9.66%) of the patients in the cases group, respectively. Additionally, there was a strong correlation (p<0.05) between severe dengue patients and symptoms like lethargy, vomiting, diarrhoea, and abdominal discomfort. Abdominal pain, diarrhoea, vomiting, fatigue, and nausea symptoms were reported by 84 (58.3%), 33 (22.80%), 14 (9.66%), 28 (19.44%), and 27 (18.62%) patients in the cases group, respectively Table 1.

The median values for age (median=32), hematocrit (49.62), serum creatinine (132.11), aspartate aminotransferase (AST) (171.13), alanine transaminase (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 presented in 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 in Figure 1. Additionally, the model successfully passed the Hosmer and Lemeshow goodness-of-fit test value is 10.46 with degrees of freedom 8 (P= 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 risk28,29. 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 15,30,31 and other countries 32,33. 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 34–38 and previous studies in Bangladesh 2,30. 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 15,31,39–41​. 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, it was reported that the presence of headache upon presentation was linked to reduced odds of developing DHF 36.

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 is limited to 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.

**Ethical Considerations**

Before commencing the data collection ethical approval was taken from the Institutional Ethical Research Board of President Abdul Hamid Medical College and Hospital (*Ref: IERB/PAHMCH/2023/P04, dated 19 December 2023*). Patient written consent was taken accordingly, and they were informed about the study’s objectives.

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**Data Availability Statement:** Data will be made available upon reasonable request.

**Conflicts of Interest:** The authors declare no conflicts of interest.

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**Author’s Contributions**

**KF:** Writing – review & editing

**MNH:** Formal analysis, Investigation, Methodology, Project administration, Software, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing

**MNA:** Supervision, Data curation, Investigation

[Conceptualization, Data curation, Investigation, Methodology, Project administration]

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**Table1. Association of socio-demographic characteristics, signs-symptoms and comorbidities**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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** |  |  |  |  |
| 12 years or above | 7 (4.96) | 7 (2.46) | 14 (3.29) | 0.316 |
| 10 years | 27 (19.15) | 50 (17.61) | 77 (18.12) |  |
| 5 years | 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 Findings between Dengue Cases and Controls

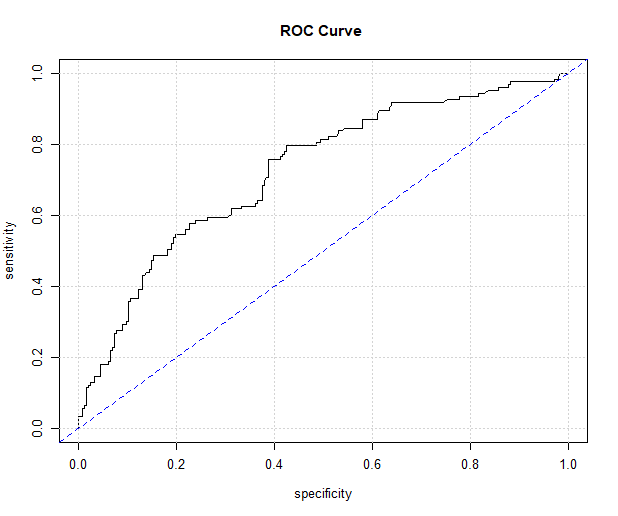
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variables** | **Cases**  **Median (IQR)** | **Controls**  **Median (IQR)** | **Totals**  **Median (IQR)** | ***p*-value** |
| **Age (Years)** | 32 (22) | 25 (15) | 27 (19) | <0.001 |
| **WBCs (cells × 109 /L)** | 4.90 (2.37) | 5.51 (3.50) | 5.20 (3.12) | <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, signs and symptoms comorbidities**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure variables** | **Univariate Logistic** |  | **Multivariate**  **Logistic** |  |
|  | **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% | |



**Fig 1. Goodness of fit and accuracy of the final model**

**Table S1:** STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

|  |  |  |  |
| --- | --- | --- | --- |
|  | Item No | Recommendation | Page No |
| **Title and abstract** | 1 | (*a*) Indicate the study’s design with a commonly used term in the title or the abstract | 01 |
| (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 02 |
| Introduction | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 03-05 |
| Objectives | 3 | State specific objectives, including any prespecified hypotheses | 05 |
| Methods | | | |
| Study design | 4 | Present key elements of study design early in the paper | 05 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 05 |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants | 06 |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 06 |
| Data sources/ measurement | 8\* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 06-07 |
| Bias | 9 | Describe any efforts to address potential sources of bias | N/A |
| Study size | 10 | Explain how the study size was arrived at | 05 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 06 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 06 |
| (*b*) Describe any methods used to examine subgroups and interactions | 06 |
| (*c*) Explain how missing data were addressed | 06 |
| (*d*) If applicable, describe analytical methods taking account of sampling strategy | 06 |
| (*e*) Describe any sensitivity analyses | 07 |
| Results | | | |
| Participants | 13\* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 08-09 |
| (b) Give reasons for non-participation at each stage | N/A |
| (c) Consider use of a flow diagram | N/A |
| Descriptive data | 14\* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 08-09 |
| (b) Indicate number of participants with missing data for each variable of interest |  |
| Outcome data | 15\* | Report numbers of outcome events or summary measures | 08-09 |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 08-09 |
| (*b*) Report category boundaries when continuous variables were categorized | N/A |
| (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | N/A |
| Other analyses | 17 | Report other analyses are done—eg analyses of subgroups and interactions, and sensitivity analyses |  |
| Discussion | | | |
| Key results | 18 | Summarise key results concerning study objectives | 09-10 |
| Limitations | 19 | Discuss the limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 11 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 09-11 |
| Generalizability | 21 | Discuss the generalizability (external validity) of the study results | 09-11 |
| Other information | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 12 |