Impact of Comorbid Conditions on Severity of Dengue Fever: A Comparative Study

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ABSTRACT

Objective: to identify the comorbid conditions associated with an increased risk of severe Dengue in clinically diagnosed patients with Dengue viral infections.

Study Design: Comparative cross sectional study.

Place and Duration of Study: Dengue ward, Department of Medicine, Combined Military Hospital Lahore, from Oct to Nov 2021.

Methodology: Three hundred patients with confirmed Dengue infection were enrolled in the study. These patients were divided into two groups: 150 patients with comorbids (diabetes mellitus, hypertension, ischemic heart disease) and 150 patients without comorbids. The impact of comorbid conditions on the severity of dengue fever was studied.

Results: Seventy-three out of the 300 patients had Dengue Fever without warning signs, while 79 out of the 300 patients had Severe Dengue Fever. Almost half of the patients (148) 300 had Dengue Fever with warning signs. The mean age of participants is 45.62±14.06 years. Patients with diabetes mellitus were more likely to develop Dengue without warning signs. Patients with hypertension were more likely to develop severe Dengue.

Conclusion: This study showed that comorbid conditions such as Diabetes and Hypertension are important risk factors for developing severe Dengue.

Keywords: Dengue fever, Diabetes mellitus, Hypertension.

INTRODUCTION

Dengue fever has been the most important mosquito-borne viral infection in recent years. Its incidence has been increasing worldwide, resulting in a great public health burden, especially in South-East Asia and Western Pacific Regions.[1] These areas are estimated to be nearly two-thirds of the global dengue disease burden. The number of dengue cases reported to WHO increased overfold in the last two decades, from 505,430 cases in 2000 to over 2.4 million in 2010 and 5.2 million in 2019.[2] Reported deaths between 2000 and 2015 have increased from 960 to 4032, in which younger patients were mostly affected. In the tropical and subtropical regions, 3 billion people are at risk of infection, 96 million have symptomatic infections, and 20,000 deaths occur yearly.[3,4]

It has been studied that certain conditions predispose patients to severe forms of Dengue; these include Hypertension, Diabetes Mellitus, Ischemic Heart Disease, Chronic Renal Failure and old age.[5,6] Therefore, understanding the impact of comorbidities in developing severe Dengue is important for better management and clinical outcomes.[7]

Endothelial dysfunction plays an important role in the pathogenesis of severe Dengue. Conditions such as Diabetes Mellitus are associated with endothelial disruption and dysfunction due to an activated immune response and increased cytokine release.[8] Patients with diabetes are more likely to develop severe Dengue. It is also seen that patients having Diabetes Mellitus with Hypertension had an increased risk of developing Severe Dengue as compared with patients with Diabetes Mellitus and no Hypertension, further suggesting endothelial dysfunction is an important cause in pathogenesis.[9,10] The objective of this study is to identify the comorbid conditions associated with an increased risk of severe Dengue in clinically diagnosed patients with Dengue viral infections.

METHODOLOGY

The comparative cross-sectional study was conducted at the Dengue ward, Department of Medicine, Combined Military Hospital Lahore, from October to November 2021 after approval from Ethical Committee (certificate number: 345/2021). The WHO sample size calculator was used for sample size estimation. Non-probability consecutive sampling was done.

Inclusion Criteria: Patients of either gender, aged 14 to 78 years, with or without comorbid conditions with

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confirmed Dengue infection based on Dengue NS-1 Antigen and/or Dengue IgM and classified according to revised WHO 2009 criteria were included in this study.

Exclusion Criteria: Patients with fever other than Dengue infection based on history and investigations were excluded from this study.

Case definition of Dengue viral Infection was according to WHO 2009 criteria (Dengue patients with and without warning signs, who live in/travel to dengue endemic areas and have fever and 2 of the following criteria: nausea, vomiting, positive tourniquet sign, leukopenia, and any warning sign (abdominal tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleed, lethargy, liver enlargement >2cm, laboratory tests: increase HCT with decrease in platelets).[11] Patients with severe Dengue were those with severe plasma leakage leading to shock, fluid accumulation, and respiratory distress. Severe bleeding was evaluated by the clinician. Severe organ involvement was Liver AST or ALT >1000, CNS: impaired consciousness, heart and other organs. Three hundred patients with confirmed dengue infection (150 with comorbid conditions and 150 without any comorbid) were enrolled in the study after obtaining informed consent and divided into two groups. Then, the severity of Dengue Infection was compared in both groups.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Pearson correlation coefficient test was used for correlations, and *p*-value ≤0.05 was considered as statistically significant.

RESULTS

A total of 300 patients diagnosed with Dengue fever were enrolled in the study. The mean age of participants was 45.62±14.06 years. Just under a quarter of the patients, 73(24%), had Dengue fever without warning signs, while 79(26%) had severe Dengue fever. Almost half of the patients, 148(49%), had Dengue fever with warning signs. Co-morbid distribution has been tabulated in Table-I. There were 53 patients with Dengue without warning signs and a single co-morbid condition. Of these patients, 15(28%) had DM, while 24(45%) had HTN. In addition, 14(26%) had IHD (Table-II). A total of 112 patients who had Dengue with warning signs and a single co-morbid condition. Among them, 52(46%) had DM, 43(38%) had

HTN and only 17(15%) had IHD (Table-III). Fifty-two patients with Severe Dengue and had single co-morbid out of the three mentioned co-morbid conditions, 28(54%) had DM while 11(21%) had HTN and 13(25%) had IHD (Table-IV).

Table-I: Co-morbid Distribution among the Patients (n=300)

Co-morbid Condition	n(%)
Patients with no co-morbid	149(46.7%)
Patients with Diabetes Mellitus only	55(18.3%)
Patients with Diabetes Mellitus and Hypertension only	16(5.3%)
Patients with Diabetes Mellitus and Ischemic Heart Disease only	4(1.3%)
Patients with Diabetes Mellitus, Hypertension and Ischemic Heart Disease	20(6.7%)
Patients with Hypertension only	36(12.0%)
Patients with Hypertension and Ischemic Heart Disease only	6(2.0%)
Patients with Ischemic Heart Disease only	14(4.7%)

Table-II : Correlation between the co-morbid Condition and Dengue without Warning Signs (n=53)

Co-Morbid Condition	n	r-value	*p*-value
Diabetes Mellitus	15	-0.136	0.019
Hypertension	24	0.089	0.124
Ischemic Heart Disease	14	0.072	0.210

Table-IV: Correlation between Co-morbid Condition and Severe Dengue (n=52)

Co-Morbid Condition	n	r-value	*p*-value
Diabetes Mellitus	28	0.049	0.400
Hypertension	11	-0.165	0.004
Ischemic Heart Disease	13	0.030	0.583

DISCUSSION

Our study aimed to identify comorbidities that would predict the development of severe Dengue in patients suffering from them. Our study found a strong statistical association between certain comorbidities and the development of severe Dengue. Diabetes mellitus was found to be an independent risk factor for developing Dengue without warning signs (*p*-value 0.019), and hypertension had a stronger association with severe Dengue (*p*-value=0.004). Studies of dengue patients from different areas have reported a similar pattern, showing an increased risk of severe Dengue in comorbidities.[11] In a study done by Latt *et al*. there was no significant association of diabetes with severe dengue fever according to both WHO 1997 and 2009 guidelines (*p*=0.109 and 0.187, respectively).[12]

In a study done by Mirza *et al*. during the dengue epidemic in 2011 in Lahore, it was found that Diabetes

mellitus is a strong risk factor for DHF or severe Dengue (OR=2 0.146, CI 1.52-3.013), and diabetes along with hypertension had a stronger association with DHF (OR 3.56; CI 1.96-6.49).[13] In a Brazilian study by Figueiredo *et al.*, significant associations were found between severe Dengue and diabetes (OR=2.75; CI 1.12–6.73). Patients treated for hypertension had a 13 times higher risk of severe Dengue than patients with no hypertension. (OR 1.65 CI: 1.23-2.441.[14] In the past, studies have been done that showed increased morbidity and mortality in patients suffering from severe Dengue with comorbid conditions such as ischemic heart disease, diabetes and hypertension.[15-17]

Another study supported the role of hypertension in the progression of Dengue to severe Dengue when the subjects were using antihypertensive drugs (OR=1.4; 95% CI 1.1–2.0) and when they were not using antihypertensive drugs (OR=1.8; 95% CI 1.1–3.2).[18] Identifying comorbidities for progression to severe Dengue can help physicians triage dengue patients at admission. Our study aims to help physicians understand the diseases contributing to developing severe Dengue. Proper management and treatment of the comorbid with dengue fever would lead to better patient outcomes. By doing so, there can be a significant decrease in the number of patients developing severe Dengue, a decrease in hospital stays and a reduction in mortality.

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CONCLUSION

This study showed that comorbid conditions such as Diabetes and Hypertension are important risk factors for developing severe Dengue.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

AA: & SZ: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

FM: & KH: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

SB:, AH: & MAH: Concept, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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