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Original Research Article

Clinical profile of Dengue in Indian Geriatric Population with Dengue Viral Infection

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Abstract

Background and Aim: An epidemic of dengue disease had broken out in West Bengal, India. A wide range of unusual dengue fever presentations were noted during the summer during the outbreak period. Our goal in this study was to determine the key clinical and laboratory factors that predict dengue patients' mortality.

Methods: In this prospective cross sectional observational study, 254 individuals with dengue-like fever admitted to a tertiary care hospital were examined, and the source of the fever was thoroughly probed. The ELISA method was used to measure IgM and IgG. Patients with fever from other causes were not allowed to participate in the trial. Every patient had pertinent clinical and laboratory data gathered. Using the proper statistical techniques, the relationship between clinico-laboratory parameters and mortality was investigated.

Results: Of the 254 patients, 59.4% (n = 151) were adults and 40.6% (n = 103) were old. Co-morbid disorders linked to DHF included diabetes, hypertension, and IHD; these conditions were statistically significant when compared to the adult group. The elderly cohort had a considerably higher incidence of DHF (30/130, 29.1%) compared to the adult cohort (32/151, 21.2%) (p=0.003). Similarly, SD was more common in older people (30/103, 29.1%) than in younger people (30/151, 19.9%) (p=0.005). Heart rate, systolic blood pressure, diastolic blood pressure, and respiration rate all had nonsignificant p-values (p>0.05) according to a straightforward logistic regression analysis.

Conclusion: These findings may enhance knowledge of dengue in older people. DHF, SD, and HAI are more common in elderly dengue patients, who also show atypically. For proper monitoring, early diagnosis is essential. DHF and SD are more common in elderly people, particularly those who already have concomitant conditions.

Keyword: Elderly, Dengue, dengue hemorrhagic fever, co-morbidity.

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Introduction

The most prevalent arthropod-borne viral (Arboviral) disease in humans is dengue. 2.5–3 billion people worldwide reside in 112 countries where dengue has spread. Between 50 and 100 million people contract the infection each year. It is brought on by infection with one of the four dengue virus serotypes, a Flavivirus (a genus of single-stranded non-segmented RNA viruses). A person can eventually contract all four dengue serotypes, although infection with one serotype gives lifetime homotypic immunity to other serotypes and a relatively short period of partial heterotypic immunity to other serotypes [1].

During an outbreak, multiple serotypes may be in circulation. Aedes mosquitoes, which are common in tropical and subtropical regions of the world, are the carriers of dengue. Around 2.5–3 billion people worldwide reside in 112 countries where dengue has spread. Between 50 and 100 million people contract the infection each year.

Over the years, the incidence of infection has increased, affecting over 100 million individuals annually [1, 3]. In adults, dengue typically resolves on its own. There is a higher chance of developing a serious illness when reinfection with a different serotype occurs. The WHO updated the dengue classification in 2009, making it simpler to implement from the standpoint of public health. Over the past few years, dengue epidemics have been occurring in various places of India, including Delhi, the country's capital. The National Vector Borne Disease Control Programme (NVBDCP) of

the Ministry of Health and Family Welfare, Government of India, reports that there were 129,166 dengue cases and 245 fatalities in the nation in 2016 [4].

Like any other viral infection, dengue fever manifests as fever, headache, myalgia, and other symptoms. The two most typical signs of dengue fever are thrombocytopenia and increased haematocrit, but problems can occur in any organ system. The warning signs for severe dengue have been established by the WHO. Numerous clinical and laboratory indicators have been identified in the literature as predictors of mortality in dengue fever patients. The majority of countries report a dengue case fatality rate of less than 5%, but if early detection and appropriate treatment are not provided, the percentage may rise [5–9]. Clinicians may prioritize the treatment of high-risk patients in order to lower morbidity and death if the risk variables linked to mortality were identified early. Our goal in this study was to determine the key laboratory and clinical factors that predict dengue patients' mortality.

Materials & Methods

In a tertiary care facility, a retrospective study was conducted. This study included patients over the age of eighteen who were admitted to the hospital with symptoms suggestive of dengue fever and who tested positive for IgM dengue serology. The patients gave their informed permission. The IgM Panbio kit, which has a 95% sensitivity and 94% specificity for dengue, was utilized. In all, 3254 dengue patients were enrolled in the trial, and their specific clinical and laboratory characteristics were recorded. Patients with fever from other causes were not allowed to participate in the trial.

Appropriate investigations ruled out the other usual causes of fever. For analysis, the lowest platelet count and the highest levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), prothrombin time (PT), blood urea, and serum creatinine were taken into account. Adults (19–59 years old) and the elderly (≥ 60 years old). Dengue fever, severe dengue [SD], DHF, DSS, severe hemorrhage, and severe organ involvement were among the medical interventions, diagnoses, and patient outcomes that were recorded every day in the treatment path. Laboratory, microbiological, and radiographic data were extracted from the hospital's electronic medical records. Research assistants with medical training carried out the data extraction. Patients with positive dengue reverse transcriptase polymerase chain reaction (PCR) [10] or probable dengue (WHO 1997 [11] or WHO 2009 [12]) with positive dengue IgM [13,14] met the inclusion criteria.

Fever, thrombocytopenia (platelet count<, $100*10^9$/L), bleeding (from the gastrointestinal tract, mucosa, injection sites, or other locations), and plasma leakage (clinical fluid accumulation, hypoproteinemia, increase in hematocrit of ≥20% or decrease in hematocrit of ≥20% after fluid resuscitation) were all necessary for the diagnosis of DHF according to WHO 1997 guidelines [11]. Patients with either hypotension in a patient with DHF or a fast, weak pulse with narrow pulse pressure (20 mmHg) were diagnosed with DSS [11]. According to the WHO's 2009 guidelines, SD must meet one of three criteria: severe bleeding, serious organ involvement, or significant plasma leakage [12]. Clinical fluid accumulation or a hematocrit alteration of.20% along with at least one of the following conditions was considered severe plasma leakage: tachycardia (pulse.>100/minute), hypotension (systolic blood pressure,< 90 mmHg), or narrow pulse pressure (≤20 mmHg). Hematemesis, melena, menorrhagia, or a reduction in hemoglobin necessitating a blood product transfusion were all considered severe bleeding. Hepatic damage (alanine aminotransferase.≥1000 U/L or aspartate aminotransferase.≥1000 U/L), reduced awareness, or myocarditis were examples of severe organ involvement [12].

An infection contracted more than two days after being admitted to the hospital was referred to as HAI [15]. A positive urine culture with UTI-like clinical signs was considered a urinary tract infection (UTI). A clinically relevant bacterium that was isolated from a blood culture was considered a bloodstream infection. New accumulation on a chest X-ray with corresponding clinical signs and symptoms was considered pneumonia. Positive stool Clostridium difficile toxin and diarrhea were considered signs of Clostridium difficile infection.

Statistical Analysis: Univariate associations between categorical variables were compared using the chi-squared test and Fisher's exact test, while continuous variables were compared using the Mann-Whitney U test. To determine the relationship between age and excess LOS, a multiple logistic regression model based on inpatient data was constructed. Pitt bacteremia score, HAI, Charlson co-morbidity score, and dengue severity were among the potential confounders that the model corrected for. To make sure the model fit the data correctly, the Hosmer-Lemeshow goodness-of-fit test was used.The relationship between clinico-laboratory parameters and mortality was evaluated using univariate analysis, and the risk of death was reported as Relative Risk (RR) with 95% Confidence Intervals (CI). Statistical significance was defined as a p-value of less than 0.05. The limited percentage of deaths in the study population prevented multivariable analysis from being carried out. To determine the risk factor or factors for death in the elderly patients, significant variables from univariate analyses between the fatal and non-fatal

categories were added to a multivariate logistic regression model. For the danger ratio, odd's ratio was computed. The data were analysed via SPSS software version 26

Results

The study comprised 254 patients in all who met the inclusion criteria. Males made up 74% of all patients, as Table 1 illustrates. Of the 254 patients, 59.4% (n = 151) were adults and 40.6% (n = 103) were old. Co-morbid disorders linked to DHF included diabetes, hypertension, chronic kidney disease and IHD; these conditions were statistically significant when compared to the adult group (Table 3).

Co-morbid disorders linked to DHF included diabetes, hypertension, and IHD; these conditions were statistically significant when compared to the adult group.

Table 1: The research participants' backgrounds and clinical characteristics (n=254).

Variables	Total Cases (n=254)	Adults (n=151)	Elderly (n=103)	P Value
Age (Years)	55.7 ±19.6	47.2±16.3	71.8±16.4	0.281
Gender				
Male	188 (74%)	107 (71%)	81 (78%)	0.083
Female	66 (26%)	44 (29%)	22 (22%)	
Comorbid Condition				
Diabetes Mellitus	20 (8%)	5 (3%)	15 (14%)	<0.001
Hypertension	70 (28%)	12 (8%)	58 (56%)	<0.001
COPD	8 (3%)	2 (1.3%)	6 (5.8%)	0.317
Heart Disease(IHD)	16 (6%)	1 (0.6%)	15 (14.5%)	<0.002
Chronic kidney disease	13 (5%)	1 (0.6%)	12 (11.6%)	<0.001
Laboratory diagnosis				
PCR positive only, n (%)	113 (44%)	71 (47%)	42 (41%)	0.082
Secondary dengue (IgG positive), n (%)	141 (56%)	80 (53%)	61 (59%)	0.082
Parameters at presentation				
Fever	237 (93.3%)	142 (94%)	95 (92.2%)	0.298
Malaise, lethargy	78 (30.7%)	43 (28.5%)	35 (33.9%)	0.042
Rash	110 (43.3%)	72 (47.7%)	38 (36.8%)	<0.001
Headache	108 (42.5%)	74 (49%)	36 (34.9%)	<0.001
Any aches and pain	206 (81.1%)	124 (82.1%)	82 (79.6%)	0.142
Nausea	135 (53.1%)	85 (56.3%)	50 (48.5%)	0.016
Vomiting	103 (40.5%)	64 (42.4%)	39 (37.8%)	0.206
Mucosal bleeding	50 (19.7%)	37 (24.5%)	13 (12.6%)	<0.001
Hematuria	3 (1.1%)	1 (0.6%)	2 (1.9%)	0.047
Melena	15 (5.9%)	1 (0.6%)	14 (13.6%)	0.215
Leukopenia	181 (71.2%)	115 (76.1%)	66 (64%)	<0.001
Dengue virus serotype				
Serotype 1	4 (1.5%)	3 (2%)	1 (1%)	0.02
Serotype 2	224 (88%)	131 (87%)	93 (90%)	0.106
Serotype 3	25 (9.8%)	16 (11%)	9 (9%)	0.108
Serotype 4	1 (0.4%)	1 (0.6%)	0	1
Vital Signs				
Heart Rate	90.69 ± 18.66	86.64 ± 14.92	91.47 ± 19.23	0.082
Systolic blood pressure (SBP)	127.50 ± 28.14	126.72 ± 24.31	129.21 ± 26.43	0.109
Diastolic blood pressure (DBP)	86.38 ±9.21	85.67 ±9.14	86.72 ±9.66	0.291
Respiratory Rate (RR)	20 ± 2	18 ± 2	20 ± 2	0.314

Thrombocytopenia was the most prevalent abnormality observed in every patient, as indicated in Table 2. The lowest platelet count exceeded 1,00,000 cells/mm3 in just 25 (10%) of the patients.

171 (67%) and 121 (47%) of the patients had elevated AST and ALT, respectively. Thirty-five (14%) of the patients had renal failure. None of these individuals needed hemodialysis, and the majority experienced just slight increases in blood urea and/or serum creatinine.

Thirteen (5%) of the patients showed altered sensorium as a sign of encephalopathy. Twenty-one (8%) individuals had multi-organ dysfunction.

Table 2: Study participants' laboratory parameters (n=254)

Variables		N(%)
Hematocrit (%)	≤ 50	136 (53.5%)
	>50	118 (46.5%)
Leucocyte Count (cells/mm^3)	< 4000	43 (17%)
	4001-11000	178 (70%)
	>11000	33 (13%)
Platelets (cells/mm^3)	< 10000	16 (6%)
	10001-19999	51 (20%)
	20000-49999	76 (30%)
	50000-99999	86 (34%)
	≥100000	25 (10%)
AST (U/mL)	<40	83 (33%)
	40-199	114 (45%)
	≥200	57 (22%)
ALT (U/mL)	<40	133 (52%)
	40-199	89 (35%)
	≥200	32 (13%)

Table 3 displays clinical results. The elderly cohort had a considerably higher incidence of DHF (30/130, 29.1%) compared to the adult cohort (32/151, 21.2%) (p=0.003). Similarly, SD was more common in older people (30/103, 29.1%) than in younger people (30/151, 19.9%) (p=0.005). ICU admission and mortality did not change significantly between adult and elderly dengue patients, despite the latter having more severe illness. Compared to adults (1/151, 0.6%), HAI was more common in the elderly (4/103, 3.8%). Notably, the most prevalent HAIs were pneumonia and UTIs. While there was one case of bloodstream infection in adults compared to none in the elderly, this difference was not statistically significant. One adult patient was found to have a Clostridium difficile infection. After controlling for HAI, Charlson score, Pitt bacteremia score, and dengue severity, older patients were more likely to be hospitalized for longer.

Table 3: Results for adult and elderly dengue fever patients

Parameters	Adults (n=151)	Elderly (n=103)	P Value
Dengue severity			
DHF	32 (21.2%)	30 (29.1%)	0.003
DHF Grade I–II	26 (17.21%)	29 (28.2%)	<0.001
DSS	5 (3.31%)	2 (1.9%)	0.061
SD	30 (19.9%)	30 (29.1%)	0.005
SD criteria			
Severe bleeding	9 (5.9%)	5 (4.8%)	0.002
Severe plasma leakage	7 (4.6%)	6 (5.8%)	0.209
Severe organ involvement	4 (2.6%)	4 (3.8%)	0.11
SB+SPL	3 (1.9%)	2 (1.9%)	0.692
SB+SOI	1 (0.6%)	1 (0.9%)	0.439
SPL+SOI	2 (1.3%)	4 (3.8%)	<0.001
SB+SPL+SOI	1 (0.6%)	1 (0.9%)	0.101
Outcome			
ICU	2 (1.3%)	1 (0.9%)	0.054
Death	0	1 (0.9%)	1
HAI			
Any HAI	1 (0.6%)	4 (3.8%)	<0.001
Pneumonia	1 (0.6%)	4 (3.8%)	<0.001
UTI	3 (1.9%)	2 (1.9%)	0.002
Clostridium difficile	1 (0.6%)	0	1
Bloodstream infection	1 (0.6%)	0	1

DHF = dengue haemorrhagic fever, DSS = dengue shock syndrome, SD = severe dengue, SB = severe bleeding, SPL = severe plasma leakage, SOI = severe organ involvement, ICU = intensive care unit, HAI = hospital acquired infection, UTI = urinary tract infection.

The findings of the basic logistic regression analysis for the relationships between clinical symptoms and elderly dengue fever patients are displayed in Table 4. Heart rate, systolic blood pressure, diastolic blood pressure, and respiration rate all had nonsignificant p-values ($p>0.05$) according to a straightforward logistic regression analysis. A significant correlation was found between blood parameters and hospitalized elderly patients with dengue fever (b = 0.03, crude OR (95% CI) =1.03 (1.02, 1.05), $p<0.001$). The crude OR was 1.03, meaning that older individuals had a 3.0% higher chance of infection for every unit rise in their AST measurement. ALT was another variable that was found to have a strong correlation. According to the crude OR (95% CI) = 1.03 (1.01, 1.05), b = 0.03, and $p<0.001$, patients have a 3.0% higher chance of being infected for every unit increase in their ALT value.

Table 4: Association between vital signs and blood parameters in geriatric patients with dengue fever (n = 103)

Variable	Regression coefficient (b)	Wald-statistic (df)	Crude OR (95% CI)	P Value
Heart Rate	0.02	1.85 (1)	1.02 (0.99,1.04)	0.182
Systolic blood pressure (SBP)	0.00	0.00)1)	1.00 (0.99,1.02)	0.989
Diastolic blood pressure (DBP)	0.01	0.41 (1)	1.01 (0.98,1.04)	0.531
Respiratory Rate (RR)	0.20	3.64 (1)	1.22 (1.00,1.49)	0.064
Platelet	-0.00	3.60 (1)	1.00 (0.99, 1.00)	0.061
AST	0.03	18.38 (1)	1.03 (1.02. 1.05)	<0.001
ALT	0.03	13.44	1.03 (1.02. 1.05)	<0.001

Discussion

Elderly patients are increasingly being affected by dengue, a neglected tropical illness. Dengue in the elderly is predicted to become widespread as the epidemic develops and the population ages. This group may present atypically, making diagnosis difficult. Lifesaving treatments may be postponed if a diagnosis is delayed. With higher rates of DHF, SD, and dengue-related death, elderly patients have worse outcomes than their younger counterparts. Due to their greater rates of HAI, elderly individuals are more vulnerable to infection-related death. Due to severe illness, comorbidity, and HAI, hospital stays for elderly people are longer. The already overburdened hospital systems would be further burdened by this.

According to earlier research, older patients had considerably greater incidence of DHF and SD and worse clinical outcomes [16,17]. In contrast to Puerto Rico [17] and Taiwan [12,18], this did not lead to an increase in mortality in our study. Given that the older cohort had more severe illness, the causes of this are unknown. Severe bleeding and plasma leakage were common signs of SD in the elderly. The elderly did not exhibit greater warning signs despite having more severe diseases. No single warning sign was very sensitive in predicting either DHF or SD in adult patients with confirmed dengue [19]. However, the development of both DHF and SD is extremely selective for hepatomegaly, continuous vomiting, hematocrit rise coupled with rapid platelet decline, and clinical fluid accumulation. In contrast to Puerto Rico [17] and Taiwan [18], this did not lead to an increase in mortality in our study. Given that the older cohort had more severe illness, the causes of this are unknown. Hepatomegaly was far more common in the elderly in our sample. It is necessary to be vigilant for the aforementioned warning signals in the elderly in order to guarantee the delivery of potentially life-saving measures. However, it is important to acknowledge the limitations of warning indicators in order to avoid being misled in their absence.

Secondary dengue infections are more likely to cause DHF, which is characterized by bleeding and plasma leakage [20]. An important risk factor for prior dengue infection in Singapore is advanced age [21]. In a seroepidemiologic examination of adults, 17.2% of young adults (18–24 years old) and 88.9% of those aged 55–74 exhibited evidence of prior infection [21]. This information suggests that many of the elderly patients in our group had secondary dengue infections, which raised their chance of developing DHF [18].

Comorbidities may contribute to higher rates of DHF in the elderly. Elderly patients in our cohort had considerably higher rates of diabetes and hypertension, two conditions known to be risk factors for DHF [22]. Adult patients with concurrent diabetes and hypertension had a greater chance of developing DHF than patients without these comorbidities, according to a case-control study of DHF and dengue patients in Singapore [22]. Diabetes mellitus causes both concurrent immunosenescence [13] and immunological dysfunction [23], while the pathophysiology underlying this link is unknown. Elderly dengue patients with diabetes should be admitted for intensive observation since early management with fluid treatment may save their lives.

Among elderly patients with dengue fever, multiple logistic regression analysis showed a strong correlation between the platelet count and infection. This study is in line with a retrospective observational study conducted in Kerala, India, which found that the most common haematological abnormality was thrombocytopenia (platelet count $<150x10^9$ /L), followed by leukopenia (total white blood cell count $<4x10^3$ /mm^3) [24]. Our retrospective study has several limitations.

First, patients may have received empirical treatment without clinical evaluation, which could account for the underreporting of HAI. Second, the use of intrusive devices like urinary and intravenous catheters can raise the risk of HAI. It is unknown how many patients in this study had invasive devices before HAI started. Thirdly, because the investigation was carried out at a single medical facility, referral patterns may have influenced the severity of sickness. To improve our knowledge of the variables influencing hospital admission and outcome, future research should include older patients who are handled in the community.

Conclusion

Elderly dengue is a new phenomenon that is still poorly understood. When diagnosing fever in older individuals with appropriate epidemiological exposure, dengue should be taken into consideration. Additionally, because this group presents atypically, diagnostic testing should be taken into consideration. For proper monitoring, early diagnosis is essential. DHF and SD are more common in elderly people, particularly those who already have concomitant conditions. In order to closely follow this population, a lower hospital admission threshold might be necessary. Because HAIs are more common in older dengue patients and can raise mortality risk, clinicians must be on the lookout for them.

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