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CLINICAL PRESENTATIONS OF DENGUE PATIENTS WITH DIFFERENT SEROTYPES

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ABSTRACT

Dengue fever, or dengue hemorrhagic fever, is a major global health concern. Infection with two distinct serotypes of the dengue virus may cause severe disease and even death. From the total number of confirmed cases (4,743), 50.6% (2,398) had a distinct Dengue serotype. The most common serotype was DEN-3 (50.6%), followed by DEN-1 (25.7%), DEN-2 (20.9%), and DEN-4 (2.7%). There was no distinction between the sexes. Patients in DEN-4 were substantially older than those in DEN-1, DEN-2, and DEN-3 (mean ages 9, 8, and 8, respectively). While DEN-1, DEN-2, and DEN-3 were most common in children aged 5-9, DEN-4 was most common in those aged 10-14. It was shown from this research that DEN-2 infections were secondary and presented with more severe illness, as evidenced by a higher degree of plasma leakage, a higher incidence of shock, and a higher incidence of complications related to fluid overload. More individuals with aberrant increase of liver enzyme AST and ALT and a higher mean value for both AST and ALT were seen in DEN-3 and DEN-4, suggesting a greater degree of liver involvement. The incidence of hepatic dysfunction/encephalopathy was low throughout the research period since 29.6% of DEN-3 infections were primary infections and DEN-4 was an uncommon serotype. Clinical manifestations of DEN-1 tended to be the least severe, with 29.6% of cases being diagnosed as primary infections.

Keywords:DEN-2, Plasma leakage, Shock, DEN-3, DEN-4, elevation liver enzyme, AST, ALT.

INTRODUCTION

Humanity's most significant mosquito-borne viral illness is dengue. In the last 30 years, both the incidence and severity of this condition have skyrocketed. Today, nearly 2.5 billion people are in danger, mostly in tropical developing nations. Approximately tens of millions of new cases of dengue are reported each year. Among them, dengue haemorrhagic fever (DHF) accounts for hundreds of thousands of cases and is a prominent cause of hospitalization and mortality in children across many nations.

The most severe forms of the illness, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), have been linked to the DEN-2 serotype, according to several epidemiological, serological, and virological research (1,2,3). No clinical research on the clinical and laboratory manifestations of the various dengue serotypes has been performed as of yet. Accordingly, DEN-1, DEN-2, DEN-3, and DEN-4 were studied to compare these parameters.

There are four dengue virus (DENV) serotypes, or strains, that may cause dengue fever (DENV-1, DENV-2, DENV-3, and DENV-4).

2 DENV-1, DENV-2, and DENV-3, with rare instances of DENV-4, are the dengue serotypes that circulate continuously in Singapore. 3 Dengue has shifted from being a disease mostly affecting children in Singapore since the 1980s. Dengue is still widely prevalent in Singapore, where it is transmitted all year and where big outbreaks occur periodically despite extensive vector control measures. Significant epidemics first appeared in 2005 (326.5 infections per 100,000 population), mostly caused by DENV-1, and then again in 2007 (DENV-2) (192.3 cases per 100,000 population). 4 Deaths from dengue fever increased from 27 in 2005 to 24 in 2007. Deaths attributed to dengue fever fluctuated between 6 and 10 year between 2005 and 2011. Dengue virus serotypes 1 and 2 (DENV-1) are the most common, although serotypes 3 and 4 (DENV-3) are also present. 5 Despite the fact that infections of various serotypes may result in a virtually similar clinical syndrome6, there have been reports of variances in clinical presentations. These discrepancies have been attributed to changes in the underlying pathogenesis of the disease. 7,8 One notable exception is a recent big cross-sectional study of 1,716 people throughout the Americas. 9 However, there is presently no evidence to support extrapolating these results due to variations in dominant genotypes circulating in the Americas compared to this portion of the globe.

Dengue infection may cause anything from a simple case of dengue fever to life-threatening hemorrhagic plasma leak syndrome. Secondary infections, age, viral load, and infecting serotype and genotype are only few of the characteristics that have been hypothesized to have a role in severe dengue (SD). 10–13 Dengue has been reported in children before, and studies have shown that secondary DENV-2 infection is associated with more severe illness than infection with other serotypes. 14–17 Cases of main DENV-1 were more noticeable, but those of DENV-2 and DENV-3 were often underreported. 18,19 Furthermore, published phylogenetic data imply that the Asian genotype of DENV-2, rather than the Cosmopolitan genotype circulating in Singapore, is prevalent in these research, with uncertain implications for disease presentation. 20,21 Phylogenetic analyses of the DENV envelope protein gene have shown that even across DENV serotypes, there is substantial variation resulting in a wide range of genotypes with distinct pandemic potentials. 22 Different dengue viruses circulate over the world, and doctors in non-endemic areas need to know how to treat febrile returning travelers infected with one of these viruses based on the serotype and molecular differences between them.

The DENV genome is roughly 10,600 nt in length, and is a single-stranded, positive-sense RNA with a single open reading frame (ORF) and two untranslated regions (UTRs) on each end (Rice et al, 1985). Three structural proteins—core (C), membrane (M), and envelope (E)—and seven non-structural proteins make up a DENV virion (Chambers et al, 1990). DENV is a virus with four different serotypes: DENV-1, DENV-2, DENV-3, and DENV4. DHF pathophysiology has been linked to amino acid variations among DENVs (Mangada and Igarashi, 1998; Pandey and Igarashi, 2000).

The E protein of dengue viruses contains the vast majority of neutralizing epitopes (Roehrig et al, 1998). Virus attachment to host cells and fusion of virions with host cell membrane are both facilitated by E protein (Crill and Rochrig, 2001), and the E protein sequence of DENV4 is remarkably stable (Patil et al, 2012). There are periodic dengue outbreaks in Indonesia, but little studies on the variety of DENVs identified there, notably DENV-4 (Personal observation: only 4 strains of DENV-4 have been deposited in GenBank). All DENV serotypes are endemic in Jakarta, but DENV-3 is by far the most common, as shown by an analysis of viruses identified from DHF patients in Indonesia between 1975 and 1978 and between 2005 and 2010.

LITERATURE REVIEW

Bhatt, P., Sabeena, S.P., Varma, M. et al. (2021), There is a complicated interaction between the virus, host genes, and the host immune response that contributes to the pathogenesis of dengue virus infection. Antibody-dependent enhancement (ADE), memory cross-reactive T cells, anti-DENV NS1 antibodies, autoimmunity, and genetic variables all play a role in determining disease susceptibility. The pathophysiology of severe dengue was formerly thought to be due to the NS1 protein and anti-DENV NS1 antibodies. Sequential infection with distinct DENV serotypes may modify the cytokine response of cross-reactive CD4+ T cells, leading to additional elevation of pro-inflammatory cytokines resulting to a worse immune response. Vascular endothelial cell dysfunction and increased vascular permeability come from the release of cytokines from immune cells due to Fc receptor-mediated antibody-dependent enhancement (ADE). Viral determinants of illness severity include genetic diversity in the dengue virus and subgenomicflavivirus RNA (sfRNA) that inhibits the host immune response. Autoantibodies generated in response to DENV NS1antigen, DENV prM, and E proteins during a dengue infection may react with plasminogen, integrin, and platelet cells, among other self-antigens. There are several host genetic variables and gene polymorphisms that contribute to the pathophysiology of DENV infection in addition to the virus itself. Recent developments in the study of biomarkers that may one day be used to predict severe illness prognosis are discussed, as are the different elements involved for the pathogenesis of dengue.

Roy, S.K., Goswami, B.K., & Bhattacharjee, S., (2022), Northern West Bengal, often known as North Bengal, is a dengue-endemic region that has been badly impacted by Dengue in recent years, leading to significant hospitalizations and fatalities. Understanding the epidemiology of dengue fever and creating an effective vaccine depend on a complete genetic characterisation of the endemic serotypes of circulating dengue virus (DENV). The purpose of the current research was to perform a phylogenetic analysis and describe circulating dengue serotypes. All NS1-positive cases (N = 83) of patients with acute febrile sickness who were sent to various healthcare institutions had EDTA blood samples obtained and processed for RNA isolation and the generation of complementary DNA (cDNA). By focusing on the C-prM region of the virus, traditional PCR was used to identify dengue serotypes. The Maximum Likelihood approach was used to create the phylogenetic tree. Results showed that dengue virus RNA was present in 17 of 83 blood samples tested. Although DENV3 was determined to be the most common serotype in single-infection patients, we did find several serotype co-infections across the board. We observed that joint pain was the most informative sign for dengue prognosis. According to sequence analysis, all currently circulating DENV1 and DENV3 genotypes belong to the

genotype III group and are most closely connected to the Indian lineage. This is the first investigation of its kind, and may help shed light on the dengue outbreak and its etiology, by characterizing the genetic makeup of DENVs now circulating in North Bengal.

JunyaYamagishi, Lucky R. Runtuwene, Kyoko Hayashida, Arthur E. Mongan, LanAnh Nguyen Thi, (2017), The paradigm for DNA sequencing has shifted with the advent of a nanopore-type portable sequencer. It is possible to sequence materials just where they are collected. Using dengue fever as an example, we describe the invention of a new approach for detecting and genotyping microorganisms responsible for tropical diseases. We successfully amplified and sequenced our target viral genomes by using the sequencer in conjunction with isothermal amplification, which just needs a water bath. The whole process, from taking the first serum sample to the final results, may be completed in a single day. Clinical detection and serotyping of the dengue virus using this approach was shown to have good sensitivity and specificity in a study of blood samples from 141 patients in Indonesia. A total of 58 SNVs were found, with a successful detection rate of 79%. Eighty Vietnamese and twelve Thai samples were analyzed in the same way, and the results were consistent. We showed that this method may provide critical data for etiologically assessing yearly or regional diversifications of the infections based on the sequencing information collected.

According to Bharaj, P., Chahar, H.S., Pandey, A., et al (2018), Even though reports of co-circulation of several dengue virus serotypes have come in from numerous countries, including India, it is still unusual to find evidence of simultaneous infection with both serotypes. Dengue fever/dengue shock syndrome (DHF/DSS) broke out in and around Delhi in 2006. This is the first report of a widespread epidemic of several dengue virus serotypes in India at the same time. Patients' acute phase serum were analyzed using RT-PCR to detect the presence of dengue virus RNA. The detection rate for dengue virus RNA in the 69 samples was 69.5%, meaning that 48 of the 69 samples were positive. In this epidemic, DENV-3 was the most common yet all four serotypes of dengue virus were present. In addition, co-infection with two or more dengue virus serotypes was found in 9 of 48 (19%) dengue virus positive samples. Infections with several dengue virus serotypes have never before been recorded in the same epidemic outside of India. Dengue has become hyperendemic in Delhi.

B.A.M. Rocha, A.O. Guilarde, A.F.L.T. Argolo, et al (2017), From January 2012 to July 2013, 452 individuals in central Brazil with laboratory-confirmed dengue participated in a prospective trial. The clinical outcome measured the degree to which patients had mild, moderate, or severe dengue. At three distinct intervals, the patients were assessed. An in-depth examination of the dengue virus was carried out, including a blood draw for laboratory analysis and dengue virus confirmation tests. In light of the aforementioned, we conducted a multinomial analysis with the dependent variable broken down into the three groups. ORs, or odds ratios, were computed. The variables having a P-value of 0.20 or below were included into a multinomial logistic regression model. The statistical testing was done in STATA 12.0. Dengue was confirmed in 452 of 632 individuals (71.5%). In 243 of the cases, the dengue virus (DENV) serotype was determined. One hundred thirty-five patients (55.6%) were found to have DENV-4, whereas 91 (36.4%) had DENV-1, 13 (5.3%) had DENV-3, and 4 (1.6%) had DENV-2. Spontaneous bleeding (P = 0.03), severe abdominal pain (P = 0.004), neurological symptoms (P = 0.09), and thrombocytopenia (P = 0.01) were also more common in individuals with the DENV-1 serotype than in those with the DENV-4 serotype. DENV-4 had a higher rate of secondary infection (80.0%) than DENV-1

(62.3%) (P = 0.03). When compared to men, females had a greater chance of developing dengue with warning symptoms (OR = 2.12; 95% CI: 1.44-3.13; P 0.01). After accounting for differences in age and sex, the multinomial analysis revealed that the odds of developing severe dengue infection due to a secondary infection were 2.80 (95% CI: 0.78-10.00; P = 0.113) times higher than in instances of dengue fever due to a primary infection. According to the latest findings, severe dengue affected 5.8% of individuals enrolled in healthcare facilities and hospitals throughout the research period. The most common serotype in a massive dengue epidemic in central Brazil was DENV-4, followed by DENV-1. Our results provide light on the differences between DENV-1 and DENV-4 in terms of clinical manifestations and immunological state in central Brazil.

Materials and methods

We looked at medical records of dengue fever (DF) and dengue hemorrhagic fever (DHF) patients admitted to the Children's Hospital (Queen Sirikit National Institute of Child Health), Bangkok, between 1995 and 1999 who had tested positive for dengue infection via viral isolation and/or polymerase chain reaction (PCR). These laboratory verifications were conducted by the Armed Forces Research Institute for the Medical Sciences (AFRIMS). The Children's Hospital relied heavily on WHO clinical criteria for making most DF and DHF diagnoses (4). While serological and virological confirmations were helpful, they were not regularly used by most practitioners. WHO criteria were also used to categorize the DHF severity.

The SPSS software was used to compare clinical and laboratory data from patients with different dengue serotypes.

Results

There were 17,908 dengue cases identified at the Children's Hospital Outpatient Clinic between 1995 and 1999, with 4,595 (or 25.7%) of those children requiring in-patient care. 4,743 patients (89.0%) underwent the serological and/or virological tests. In all, 2,398 cases (50.6%) tested positive for Dengue viruses. There were 618 DEN-1 cases (25.8%), 501 DEN-2 cases (20.9%), 1,213 DEN-3 cases (50.6%), and 64 DEN-4 cases (2.7%). Two dengue infections were found in one patient (DHF grade IV), and one dengue virus could not be diagnosed (DEN-2 and DEN-1).

In 27.5% and 29.6% of DEN-1 and DEN-3 cases, respectively, primary infections were detected, but in 5.8% and 4.7% of DEN-2 and DEN-4 cases, no such infections were present (Table 1). These data are consistent with the observation that 19.9% and 23.4% of DEN-1 and DEN-3 infections, respectively, manifested as DF (Table 2).

Table 1: Primary and secondary dengue infections

	DEN-1 (%)	DEN-2 (%)	DEN-3 (%)	DEN-4 (%)	Total (%)
Primary	27.5	5.8	29.6	4.7	23.4
Secondary	69.4	91.8	66.6	90.6	73.2

Table 2: Clinical presentations of dengue infections

	DEN-1 (%)	DEN-2 (%)	DEN-3 (%)	DEN-4 (%)	Total (%)
DF	19.9	12.8	23.4	15.6	20.1
DHF	62.5	54.3	55.8	65.6	57.4
DSS	17.6	32.9	20.8	18.8	22.5

The clinical manifestations of DHF/DSS in DEN-2 and DEN-4 were 87.2% and 84.4%, respectively, while secondary infections were detected in 91.8% and 90.6% of infections, respectively (Table 2). With 32.9% of its cases presenting as DSS, DEN-2 was substantially more common than DEN-1 (17.6%), DEN-3 (20.8%), and DEN-4 (18.2%). The largest proportion of individuals with fever after entering shock was seen in DEN-2 (22.4%).

All DEN serotypes were completely gender-neutral. Patients with DEN-4 were substantially older than those with DEN-1, DEN-2, and DEN-3 (8 vs. 8.2 vs. 8.8 years; p 0.0001). Children between the ages of 5 and 9 years old saw the highest rates of infection with DEN-1, DEN-2, and DEN-3; those between 10 and 14 years old experienced the highest rates of infection with DEN-4.

Duration of fever (4.2 days); bleeding signs [including patechiae (49.4%), epistaxis (21.4%), haematemesis (19.8%), melena (8%), gum bleeding (3.1%), and menstruation (1.6%)]; maculopapular rash (5.9%); and tourniquet test (90.5%); were all similar among all four dengue serotypes ($p>0.05$) (Table 3).

Table 3: Haemorrhagic manifestations of dengue infections

	DEN-1 (%)	DEN-2 (%)	DEN-3 (%)	DEN-4 (%)	Total (%)
Petechaie	51.9	50.6	47.9	42.6	49.4
Epistaxis	21.8	20.8	20.8	31.5	21.4
Hematemesis	19.8	22.2	18.3	27.8	19.8
Melena	8.9	8.5	8.5	9.3	8.6
Gum bleeding	3.0	3.9	2.7	5.6	3.1
Menstrua- tion	1.6	2.5	1.2	1.9	1.6

Larger livers were seen in individuals with DEN-2 (92.7%) and DEN-3 (93.3%) compared to those with DEN-1 (88.9%) and DEN-4 (85.2%).

None of the four dengue serotypes were particularly associated with unusual symptoms. For all four serotypes (0.8%), the same proportion of patients presented with encephalopathy: DEN-1 (0.6%), DEN-2 (1.2%), DEN-3 (0.7%), and DEN-4 (1.6%). All dengue serotypes had the similar rates of associated infections (3.9%) and conditions (3.3%). (Table 4).

Table 4: Unusual manifestations of dengue infections

	DEN-1(%)	DEN-2(%)	DEN-3(%)	DEN-4(%)	Total(%)
Encephalopathy	0.6	1.2	0.7	1.6	0.8
Associatedinfections	4.0	3.4	4.2	0	3.9
Associatedconditions	4.4	2.3	3.3	0	3.3

The highest mean rising haematcrit (Hct) was the highest in DEN-2 (21.5%) and the lowest in DEN-3 (17.8%). The mean WBC was the highest in DEN-2 (4,440 cells/cumm.) and the lowest in DEN-1 (3,585 cells/cumm.). The mean platelet count was the lowest in DEN-2 (62,178 cells/cumm.) and the highest in DEN-1 (72,078 cells/cumm.) (Table 5).

Table 5: CBC in dengue infections

	DEN-1(%)	DEN-2(%)	DEN-3(%)	DEN-4(%)	Total(%)
Mean Hct maximum	43.3	45.0	42.7	43.8	43.4
Mean Hct minimum	36.4	36.9	36.1	36.7	36.4
Mean rising Hct	18.8	21.5	17.8	20.1	18.9
MeanWBC (cells/cumm)	3,585	4,440	3,992	3,991	3,984
MeanPMN	52	48	41	49	45
Mean AL	7	7	8	8	7
Mean Pltcount (cells/cumm)	72,078	62,178	75,502	66,565	71,592

Patients with DEN-3 had the greatest mean AST (272 U), followed by those with DEN-1 (195 U), DEN-2 (184 U), and DEN-4 (248 U), whereas those with DEN-4 have the highest mean ALT (122 U), followed by those with DEN-1 (85 U), DEN-2 (77 U), and DEN-3 (248 U) (114 U). Patients infected with DEN-1 had an AST rise of 30.2%, DEN-2 of 19.3%, DEN-3 of 36.4%, and DEN-4 of 37.1%. Patients infected with DEN-1 had an ALT rise of 9.2%, DEN-2 of 6.3%, DEN-3 of 13.7%, and DEN-4 of 20.4%. (Table 6).

Table 6. Percentage of dengue patients with elevation of AST/ALT > 200 U

	DEN-1(%)	DEN-2(%)	DEN-3(%)	DEN-4(%)	Total (%)
AST	30.2	19.3	36.4	37.1	30.9
ALT	9.2	6.3	13.7	20.4	11.2

During the critical phase, patients in DEN-1, DEN-2, DEN-3, and DEN-4 received 71 ml/kg, 83 ml/kg, 71 ml/kg, and 66 ml/kg of IV fluid, crystalloid solution, and 17, 19 ml/kg, colloidal solution, of Dextran-40, respectively.

Patients with DEN-1, DEN-2, and DEN-3 were transfused blood at rates of 5.3%, 6.7%, and 5.6%, respectively. In this analysis, DEN-4 patients did not have a significant need for transfusions. The percentage of DEN patients who had fluid overload complications ranged from 4.4% in those with DEN-1 to 9.6% in those with DEN-2 to 5.4% in those with DEN-3 to 1.9% in those with DEN-4.

All four dengue serotypes had an identical case-fatality rate (CFR; p=0.981). At 0.4%, 0.5%, and 0.3% for DEN-1, DEN-2, and DEN-3, respectively, the CFR values were very low. Patients with DEN-4 had a 100% survival rate.

Dengue serotype

Dengue infection was verified in 72 percent of 190 individuals who met the criteria for inclusion, with DENV-2 being the most common strain (Dewi et al, unpubished). Only 16 people were infected with DENV-4; 11 of them had only contracted DENV-4 (69%), while the remaining 5 had also contracted one or more of the other DENV serotypes (Fig 1). For example, eight out of ten individuals infected with DENV-4 alone had only moderate illness (DF), but those co-infected with another DENV serotype (s) had much more severe disease (Table 2). While coinfection with DENV-4 and DENV-1 resulted in DF in 2 instances (67%), coinfection with DENV-4 and DENV-2 exhibited clinical manifestation of DHF grade I, and co-infection with 3 serotypes (DENV-1, DENV-3, and DENV-4) resulted in clinical manifestation of DHF grade II. If you use the HI test, you'll see that all mixed DENV infections were secondary infections.

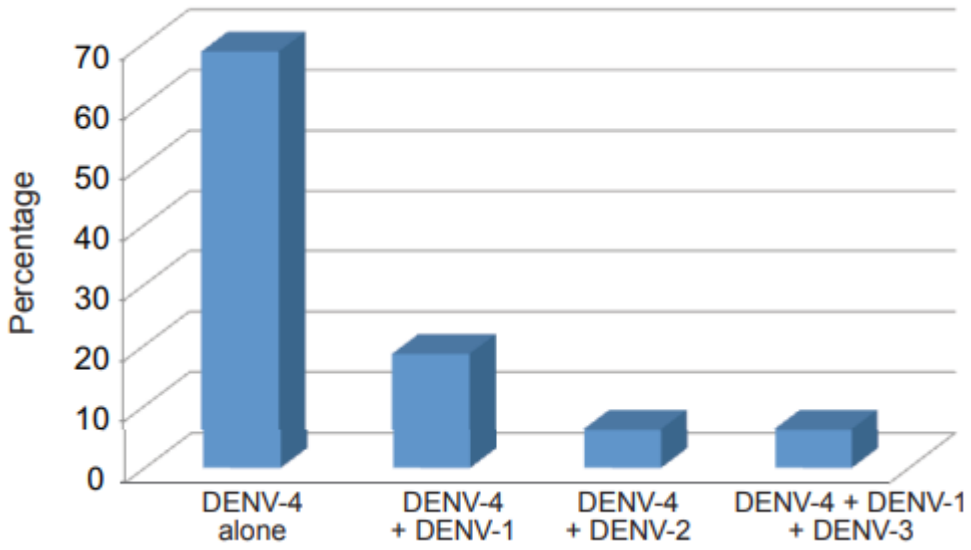

Fig 1–Prevalence of DENV-4 and co-infection in dengue patients in Jakarta, Indonesia

Discussion

Between 1995 and 1999, the percentage of cases where the dengue serotype could be identified increased from 20-30% to 50.6%. (1). This was helped along by the fact that virus detection methods have advanced. In the past, mosquito inoculation was the sole method used to isolate viruses. Identification of viruses has progressed greatly since the PCR method was first used in 1995. An even more sensitive PCR method has been used in recent years. Early admission of probable dengue patients during their feverish phase when they had viremia likely also contributed to the rise in the proportion of viral isolation/identification.

During the time span of this investigation, all four dengue serotypes were present in Bangkok. The serotype DEN-3 was the most common, whereas DEN-4 was quite uncommon. We found that DEN-1 was more prevalent than DEN-2. The severity of dengue fever in this region may depend on which serotype of the virus is more common there at any given time. This subject may be better understood by comparing the severity of the illness at times when various serotypes of dengue were prevalent.

The previously observed link between DEN-2 and a more severe version of the illness was verified; specifically, DEN-2 was shown to result in increased plasma leakage (3). This means that we need to be ready to deal with a more severe version of the illness if DEN-2 were to ever break out, which might need more colloidal and blood transfusions. Preventing complications and mortality requires prompt treatment of plasma leakage, including early identification, delivery of colloidal solution for severe plasma leakage, and blood transfusion if necessary.

Eighty percent of dengue patients, according to a prior publication, exhibited an increase in enzyme AST and/or ALT, which might be utilized as a diagnostic marker for dengue(5). High levels of AST and/or ALT were associated with DEN-3 and DEN-4 in this investigation. Primary infection with DEN-3 occurred in almost 30% of cases, while the mildest form of the illness, DF,

occurred in 23.4% of cases. These results help explain why hepatitis may be detected in certain DF patients when DEN-3 or DEN-4 is the etiological agent. Also, other DEN-3 individuals who presented with DHF were more likely to have life-threatening illness, as seen by an elevation of liver enzymes AST and/or ALT, particularly in instances of shock. We need to be ready for an increase in people with liver dysfunction or failure in the event of a DEN-3 epidemic. If a patient has an abnormal increase of these enzymes, they should go to the hospital as soon as possible, have their blood tested for AST and ALT, and be admitted as soon as possible. Such patients should use drugs very sparingly.

Similar to DEN-3, DEN-4 was more likely to affect the liver. The vast majority of DEN-4 infections (90.6%) were secondary, making DHF a probable presenting symptom. Consequently, more DHF patients with liver damage may be predicted in a DEN-4 epidemic compared to a DEN3 outbreak.

Compared to other serotypes, DEN-4 mostly affected elderly people. Due of DEN-4's historical rarity, these senior citizens may have had a head start in avoiding infection. After a period of two or three years, DEN-4 would reappear (1). If DEN-4 spreads, it is likely to infect teenagers and adults.

Aside from the higher incidence of shock following hospitalization among DEN-1 patients compared to those of other serotypes, we discovered no distinguishing features of this serotype. There was a strong relationship between shock-time WBC and illness severity. The mean WBC of DEN-2 patients was greater than that of DSS patients, while the mean WBC of DSS patients was higher than that of DEN-2 patients. If your WBC count is high, your condition is likely to be quite serious. As a basic predictor of illness severity, white blood cell (WBC) and differential counts need further investigation.

Only dengue patients who presented to the hospital early enough for the virus to be diagnosed were included in this research. Those individuals with really severe illnesses who arrived at the hospital relatively late were excluded from the trial because the virus could not be recognized after defervescence. The viruses responsible for the most severe cases of the illness need to be identified, hence a method for doing so after the viremia phase needs to be established. Incorporating data from patients who arrive at the hospital late will provide us a more complete picture of the severity of each dengue serotype.

CONCLUSION

At the Children's Hospital, dengue patients from 1995-1999 represented all four known serotypes. Serotype DEN-3 was found to be the most common (50.6%), followed by DEN-1 (25.7%) and DEN-2 (20.9%). Only 2.7% of people had the DEN-4 serotype. Evidence from a 5-year retrospective clinical and laboratory study of confirmed dengue serotypes reveals that DEN-2 is the most severe serotype, linked to secondary infections in 91.8% of cases, DHF in 87.2% of cases, and DSS in 32.9% of cases. Patients with DEN-2 required greater blood transfusions and a higher volume of intravenous fluids (both crystalloid and colloid solutions). Furthermore, DEN-2 patients were more likely to have fluid overload problems (9.6%). A larger proportion of patients with DEN-3 and DEN-4 reported rise of liver enzyme (AST and ALT) of more than 200 U, indicating a higher degree of liver involvement. Patients with DHF may be more likely to

develop liver failure quickly after experiencing a protracted shock if they have any of these conditions. Most people with DF also have hepatitis. Although DEN-1 cases were the least severe overall, they were more likely to result in hospitalization due to shock than those of any other serotype.

From these observations, we may infer the character and intensity of each dengue epidemic. There will certainly be more severe DHF cases, including shock, if a DEN-2 epidemic occurs. Clinicians need to be on high alert for patients with liver involvement during a DEN-3 or DEN-4 epidemic, and they should be ready to care for those who develop hepatic dysfunction or failure, with or without hepatic encephalopathy.

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