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Uses of antimicrobial drug in pediatric dengue virus infection of tertiary level hospital in Bangladesh

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Abstract
Background: The fastest-spreading mosquito-borne disease, dengue fever, has become a serious public health issue in tropical and subtropical countries like Bangladesh. It has been discovered that the dengue load is highest in children, adolescents, and young adults globally; babies are especially vulnerable to infection. Objective: To observe the role of antibiotics in pediatric dengue virus infection.
Methods: From July to October 2023, this cross-sectional study was conducted in the inpatient department of Bangladesh Shishu Hospital & Institute.
Results: This study included 722 hospitalized patients who tested positive for dengue in a rapid test. The largest percentage of positive patients were between the ages of 1 and 5 (38%), followed by those between the ages of 5 and 10 (32%). The most frequent symptom was vomiting (49%), followed by fever (100%). Every patient had received antibiotics, and as their hospital stay lengthened, so did the variety of medications they took. Among the administrated antibiotics, the highest percentage was levofloxacin (63), followed by meropenem (26), ceftriaxone (9), and ciprofloxacin (7) respectively. The length of the hospital stay was positively correlated with the use of multiple antibiotics. Patients with an average stay of 5 days took only one antibiotic, whereas those with an average stay of 6, 7, and 8 days used 2-4 different types of antibiotics. Among 722 patients 87 patients got Levofloxacin with Ceftriaxone and Meropenem, Ciprofloxacin with Levofloxacin and Meropenem (18), and Meropenem with Ceftriaxone and others (91) respectively.
Conclusion: The usage of antibiotics was the primary worry of hospitalized patients. We observed that giving antibiotics was the most common treatment for positive patients, and that hospital stay was strongly correlated with the quantity of antibiotics taken. A study found that giving antibiotics to dengue patients did not reduce their length of hospitalization, which sparked grave worries regarding the abuse of these medications in dengue treatment.

Keywords: Dengue, antibiotics, children

Introduction

Arboviral infections are most commonly caused by dengue [1, 2]. There are 96 million clinical cases of Dengue virus (DENV) infection worldwide, putting an estimated four billion individuals at risk. Bangladesh, a South Asian nation of over 165 million people, is one of the tropical and subtropical countries where dengue fever, the fastest-spreading mosquito-borne disease, has become a serious public health concern. Since the initial epidemic was documented in 2000, dengue has been endemic in Bangladesh. The highest dengue outbreak in Bangladesh's history occurred in 2023, with 316,773 illnesses, 1652 fatalities, and a 0.5% case fatality rate (CFR) [3]. If proper preventative strategies are not implemented, poor healthcare infrastructure, inadequate outbreak preparedness, and the lack of community-level awareness of dengue infection may lead to public health disasters [4] a dengue infection has an impact on people of all ages. Nonetheless, children, adolescents, and young adults have been found to bear the greatest burden of dengue [5]; infants in particular have the highest infection incidence [6]. Additionally, dengue infections can develop into Dengue Shock Syndrome (DSS) and Dengue Hemorrhagic Fever (DHF), which are linked to increased hospitalization and case fatality rates, especially in children [1, 2]. Fever, body aches, joint discomfort, rash, respiratory symptoms, gastrointestinal disorders, and abnormal liver function tests are the most common presentations for patients. Although less frequent, a severe form of dengue can strike some people and cause serious bleeding, organ damage, and plasma leaks, among other consequences. Life-threatening dengue shock syndrome (DSS), dengue hemorrhagic fever (DHF), and asymptomatic illness or undifferentiated fever are among the clinical manifestations of dengue virus infection [7].

Nearly every study conducted on children in Bangladesh revealed dengue's clinical symptoms at a single facility using a limited number of samples [8, 9, 10, 11]. A number of clinical symptoms have been connected to the disease's severity [12]. Dengue-associated mortality can be decreased by early detection and prompt treatment of severe dengue [13]. In light of these factors, the purpose of this study was to observe the role of antibiotics in pediatric dengue virus infection as physicians often use.

Methodology

This cross-sectional study was conducted in the in-patient Department of Bangladesh Shishu Hospital & Institute from July to October 2023. Total 722 participants who were positive for rapid test (NS1-Ag, IgM, and IgG) and age below 15 years were enrolled in this study. With the consent of the guardian and/or children's data were collected with a validated structured questionnaire and was administered to each child to elicit information on identification data, socio-demographic profile through face-to-face interviews keeping patient privacy and health settings in mind. Detailed clinical history and treatment history were also recorded. All

the data collected from the study participants was secured, and confidentiality was maintained strictly. Data were analyzed by SPSS version 26 was used for this investigation for all statistical analyses. Categorical variables were compared using $\chi 2$ tests. Figures (Bar Graphs, Pie charts, etc.) were developed using MS Excel.

Results

Detection of Dengue virus antigen and antibody using rapid kit

722 tested positives for either NS1 (667, 92%) or IgM (42, 6%). Thirteen (2%) cases tested positive for both NS1 and IgM.

Demographic and clinical distribution

Among 722 positive dengue participants, 400 were males. In terms of the patients' age distribution, 35% were between 1-<5 years old, followed by 33%, 5-<10 years, 19% from >10 years of age and 13% of participants were from <1 year. In comparison to female groups, there were comparatively more male patients in all age groups. Concerning clinical symptoms, all the participants had fever (100%), which was followed by vomiting (49%), abdominal pain (27%), loose motion (19%), and coughing (7%). Moreover, 4% of participants showed headache, 3% were reluctant to eat, 2% showed convulsions, bleeding, body aches, and rash, and 1% showed breathing difficulty.

Table 1: Demographic and clinical characteristics of dengue fever patients

Characteristics	Frequency	Percentage (%)
Age (years)		
< 1	91	13
1 - < 5	258	35
5 - < 10	238	33
≥ 10	135	19
Sex		
Male	400	55
Female	322	45
Symptoms		
Fever	722	100
Vomiting	355	49
Abdominal pain	192	27
Loose motion	135	19
Cough	49	7
Headache	30	4
Reluctant to feed	23	3
Bleeding	18	2
Convulsion	16	2
Body ache	14	2
Rash	14	2
Breathing difficulty	5	1
Warning Sign		
Yes	516	71
No	206	29

Co-morbidities and complications

We noticed that 10% (78 out of 722) of the patients had comorbid conditions, including five cases of viral hepatitis and rickettsial fever, four cases of CP, three cases of CKD and IPD, two cases of enteric IDA, epilepsy, and HTN, one case of other diseases, and seven cases of heart disease and thalassemia (Figure 1). Major consequences included shock in 17% of patients, myocarditis in 1.8%, pneumonia in 2.6%, and macrophage activation syndrome (MAS) in 3.2%. The remaining complications occurred in 1% or less of patients. Among those with shock, 85% experienced irreversible shock, 11% had compensated shock, and 4% had decompensated shock (Figure 2).

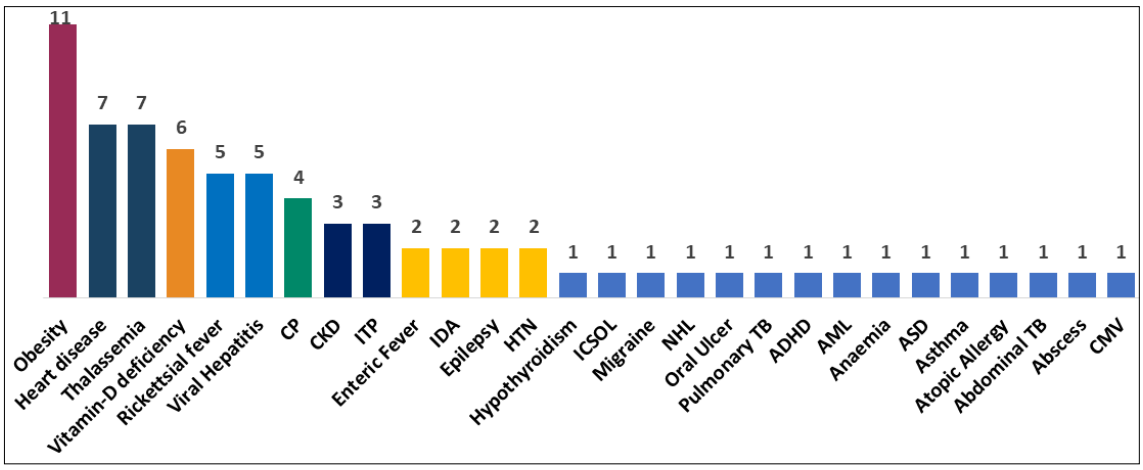

Fig 1: The distribution of Comorbid conditions among the patients

Impact of Hospital Stay on Fever Duration

The median length of hospital stay during the dengue season was 9.5 days, but 71% of patients stayed for 3–7 days. Interestingly, after ten days, the number of patients decreased, and only a few percent took more than 15 days to recover from the infections. Patients who received a diagnosis between three and six days after the onset of their fever were found to need only five days of hospitalization. Those who were tested more than six days after the onset of symptoms, however, needed to stay in the hospital for more than five days.

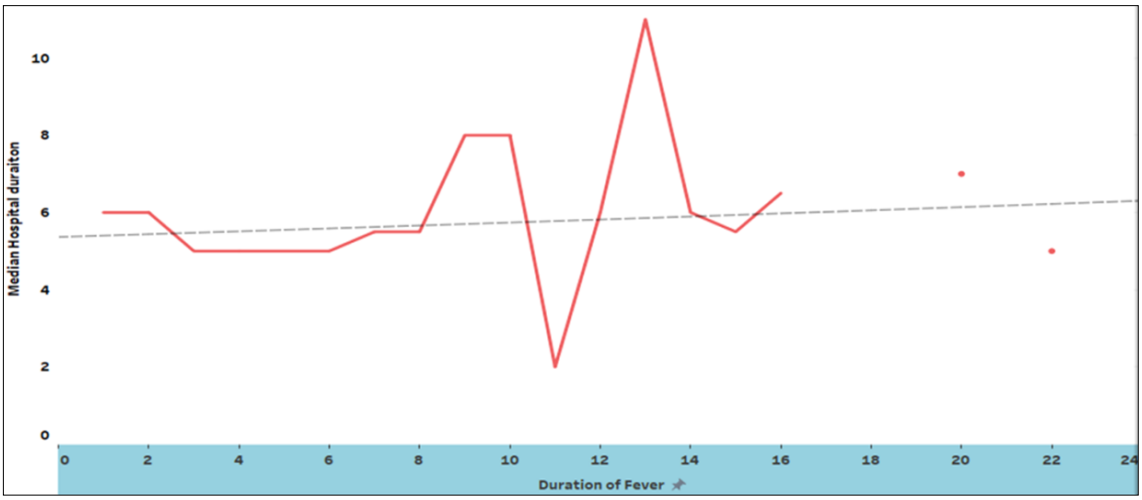

Fig 2: Impact of hospital stay on Fever Duration

Impact of Hospital Stay on Antibiotic use and Pattern of Antibiotic

Moreover, during hospital stay, 82% (n=549) patients received at least one antibiotic, 16% (n=111) two antibiotics, and 1% with 3 and 4 different types of antibiotics. Among the administrated antibiotics, the highest percentage was levofloxacin (63), followed by meropenem (26), ceftriaxone (9), and ciprofloxacin (7) respectively. The length of the hospital stay was positively correlated with the use of multiple antibiotics.

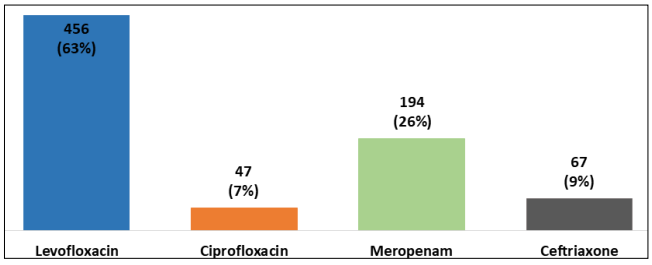

Fig 3: Pattern of antibiotic

Among 722 patients 87 patient got Levofloxacin with Ceftriaxone and Meropenem, Ciprofloxacin with Levofloxacin and Meropenem (18) and Meropenem with Ceftriaxone and others (91) respectively (Table 2).

Table 2: Combination of Antibiotics use in dengue fever patients

Antibiotics combination	Applied to the patients
Levofloxacin with Ceftriaxone and Meropenem	87
Ciprofloxacin with Levofloxacin and Meropenem	18
Meropenem with Ceftriaxone and others	91

Discussion

Dengue fever has impacted the social and economic structure of the endemic areas and is still spreading throughout the world. The current study was carried out at the pediatric hospital BSH&I between July and October 2023, during the peak of the dengue outbreak. It investigated the pattern of antibiotic use as well as clinical and demographic characteristics of children in hospitals. The majority of the clinical and demographic characteristics of this investigation are nearly identical to those of earlier studies on children in Bangladesh [5, 11, 14]. Nonetheless, the study is the first to document how hospital stays affect the use of antibiotics in Bangladesh.

Similar to another study carried out in Cameroon, we found that the majority of the positive patients were between the ages of one and five years [15]. According to the aforementioned research, newborns and young children are particularly vulnerable to dengue. Similarly, Asian national surveillance data shows that children aged four to nine and neonates under one year old have consistently had the highest risk of severe dengue disease. [16]. Children, especially neonates, are susceptible to severe dengue sickness due to their underdeveloped hemodynamic system [17, 16].

In terms of the primary symptoms, fever was the most prevalent, followed by gastrointestinal (GI) symptoms like nausea and vomiting, which appeared as warning indicators and were positively connected with the severity of Dengue patients' illness. Other studies also presented similar findings [18, 19, 20, 21]. In Bangladesh, during outbreaks in 2006 and 2008, GI symptoms were likewise seen to be the most common in youngsters [22]. In this context, the World Health Organization recommended that patients experiencing gastrointestinal symptoms be admitted to the hospital for close monitoring and the administration of intravenous (IV) fluid therapy [23]. The severity of dengue fever in this community has been shown by the study's findings that around 10% of fatality cases were among individuals who displayed warning signals. Consequently, the study proposed that lowering the disease burden requires precise detection and treatment of dengue infections.

When diagnosing dengue, we found that the rapid antibody (IgM) test only identified 6% of cases, but the rapid antigen test (NS1) identified the majority of positive cases. This implies that NS1-Ag detects positive instances more accurately.

In terms of dengue patient care, the majority of patients spent three to seven days in the hospital. According to a study, individuals with less severe conditions were likely to recover quickly and be discharged from the hospital sooner [24]. Additionally, we found that hospital stay was positively correlated with the time it took to diagnose a patient after symptoms appeared, meaning that patients who were diagnosed early needed a brief hospital stay. Another study that supported this conclusion was one by [25].

Additionally, the hospitalized patients' main concern was the use of antibiotics. We found that the most prevalent therapy for the positive cases was the administration of antibiotics, and that hospital stay was positively connected with the number of antibiotics consumed. According to a study, treating dengue patients with antibiotics did not shorten their hospital stays, which raised serious concerns about the overuse of these drugs in dengue therapy [26]. Since dengue is a viral illness, antiviral therapy may be useful in lowering the need for antibiotics, which is concerning because antibiotic resistance is becoming more widespread. In this sense, the usage of antibiotics during Dengue outbreaks ought to concern doctors more.

Conclusion

The study concludes that in order to address the high prevalence of pediatric dengue fever in Bangladesh, especially among the most affected age groups, improved management techniques, rational use of antibiotics, improved diagnostic accuracy, and focused public health initiatives are required. Since dengue fever and the deaths, it causes are currently becoming more and more of an issue in Bangladesh, the study's conclusions have significant public health ramifications.

Conflict of interest

The authors are hereby declaring that no conflict of interest exists.

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