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Original Research Article

Effect of previous episode of symptomatic dengue infection on recent dengue infection in children

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ABSTRACT

Background: Approximately 390 million people worldwide are affected by dengue fever each year, >70% of them are from Asia. It is thought that antibody enhancement during the subsequent infections with dengue virus can cause more severe form of disease called dengue haemorrhagic fever (DHF). This study aims to observe the effect of prior dengue infection on recent infection.
Methods: This retrospective record based descriptive-analytical study was conducted from July 2021 to December 2021 in paediatrics department of Bangabandhu Sheikh Mujib Medical University, Dhaka. Medical records of all admitted confirmed cases of dengue fever during the study period were reviewed retrospectively to find out past symptomatic dengue infection ,which further verified by parents over phone. Finally 98 patients were analyzed after exclusion.
Results: Among 98 studied patients, 45 (45%) experienced DHF and 15 (15.3%) diagnosed with DSS. There was no significant ($p>0.05$) difference of age and sex between patients of DF, DHF and DSS. Majority of the patients 79 (80.6%) did not have a past history of documented symptomatic dengue infection. Here, 9 (23.6%) out of 38 DF patient, 8 (17.7%) out of 45 DHF patient and only 2 (13.3%) out of 15 patient with DSS had past symptomatic dengue infection. Maximum patients (92, 93.8%) were treated with isotonic fluid, 39 patients got colloid (39, 36.79%). This study found no significant ($p>0.05$) difference between DF, DHF and DSS with or without past symptomatic dengue infection.
Conclusions: In our study we noticed that there was no increase in dengue morbidity with documented previous symptomatic dengue infection.

Keywords: Dengue, DF, DHF, DSS

INTRODUCTION

Dengue is a mosquito borne viral disease caused by four distinct serotypes of dengue virus.[1] These viruses are antigenically distinct but immunologically cross reactive. Primary vectors of dengue in the tropical region mainly include *Aedes aegypti* and *Aedes albopictus*. Approximately, 390 million dengue infection occurs each year worldwide and over 70% of total dengue infections are recorded from Asia.[2,3] In Bangladesh, over 15,000 cases of dengue are reported each year.[4] Presentation of dengue infection may be a spectrum ranging from asymptomatic to dengue fever, dengue hemorrhagic fever (DHF) and to Dengue shock syndrome (DSS).[5] Asymptomatic cases are more frequent than the symptomatic ones especially in the first infection.[6] Dengue hemorrhagic fever and DSS are associated with actively or passively acquired antibodies against dengue virus.[7]

It is believed that an infection with any serotype offers long term, if not lifelong immunity to disease due to that

serotype but only short term heterogeneous immunity to other serotypes.[8] In fact prior infection with a different DENV serotype is considered the greatest risk factor for development of severe disease like DHF and DSS in the subsequent infections. The severity is contributed by the cross reactive antibodies causing antibody mediated enhancement and also the cross reactive T cells.

The aim of the study was to observe the effect of prior dengue infection to this infection in terms of signs, symptoms and also the outcome.

METHODS

This study was a retrospective record based descriptive-analytical study conducted from July 2021 to December 2021 in paediatrics department of Bangabandhu Sheikh Mujib Medical University, Dhaka. After taking approval from Institutional Ethics Committee, to find out information about previous symptomatic dengue infection, medical records were analyzed retrospectively of all admitted confirmed cases of dengue fever during the study period. Diagnosis were confirmed on the basis of history of having high fever with either positive NS1 antigen or dengue IgM/IgG antibodies. Patients with chronic diseases or any concurrent infections were excluded. Data of 112 patient were reviewed. Finally 98 patients were analyzed for the study as 14 were excluded due to inadequate information. Information regarding prior symptomatic dengue infection not documented clearly in records was verified by parents contacting them over the phone. Diagnosis made clinically or serologically by a medical person was taken as evidence of past symptomatic dengue infection. Included children were categorized into dengue fever DF, DHF and DSS as per revised national guideline for clinical management of dengue syndrome 2018.

Haemorrhagic manifestations defined by an unusual hemorrhage, positive tourniquet test, mucosal, oral or evidence of gastrointestinal bleed; thrombocytopenia of ≤100×109/l; and objective evidence of capillary leak detected by ultrasound scan or clinical evidence of pleural effusion or peritoneal leak. The detailed demographic information including age, sex, clinical findings of current illness, evidence of past symptomatic dengue infection, complications developed during hospital stay, fluid recruitments, laboratory findings and details of clinical course of enrolled patients obtained from hospital records were recorded in a predesigned data collection sheet.

Statistical analysis

Data analysis was performed using SPSS version 20 (SPSS, Chicago, IL). The normality of continuous variables was tested with Kolmogorov-Smirnov test. The analysis of patient demographics and baseline outcome variables were summarized using descriptive summary measures: expressed as mean±standard deviation for continuous variables and frequencies and percentage for categorical variables. Appropriate statistical test (e.g. Chi-square test, Kuskalwallis test, ANOVA test) was applied for data analysis. P value<0.05 was considered as significant.

RESULTS

Total 112 children were enrolled for the study. 14 of them were excluded due to inadequate documentation in medical records. Data of 98 children were finally analyzed. Among the study population 38 (38.7%) had dengue fever, 45 patients (45%) experienced DHF and only 15 patients (15.3%) were diagnosed with DSS (Table 1).

Table 1: Distribution of cases according to severity of dengue fever (N=98).

Severity of dengue fever	N	%
Dengue fever	38	38.7
Dengue hemorrhagic fever	45	45.9
Dengue shock syndrome	15	15.3

In demographic parameters 61 (62%) were male children and there was no statistically significant (p>0.05) difference of age and sex between patients of DF, DHF and DSS (Table 2). The most common presenting features were fever 98 (100%), abdominal pain 66 (67.3%), vomiting 60 (61.2%), rash 32 (32.6%) and headache 26 (26.5%). Onset of critical phase of most the patient with severe dengue (DHF/DSS) (41/60, 68%) was managed at hospital. Whereas, about one third of them (19/60, 31.6%) admitted to the hospital at different times of the critical phase (06 hours to 36 hours from the time of onset of critical phase) with evidence of plasma leakage.

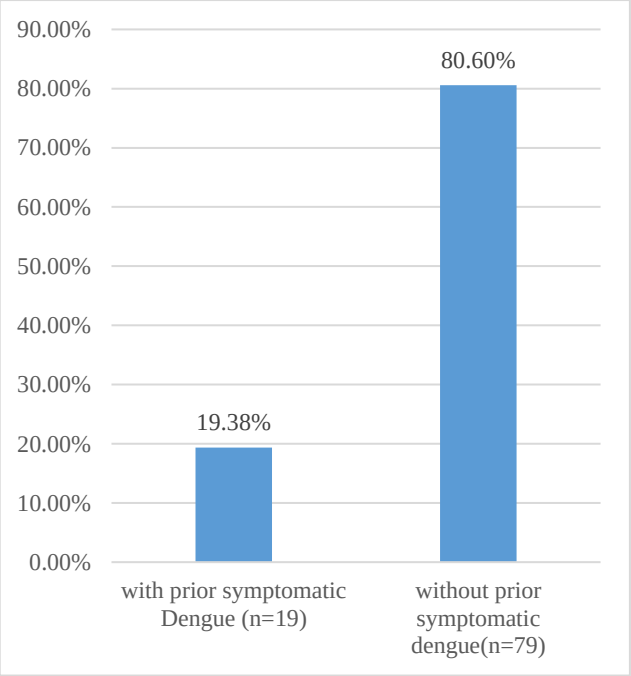

Figure 1: Distribution of study population with or without past history of symptomatic dengue infection.

Table 2: Demography of the studied children (N=98).

Variables	DF (n=38)	DHF (n=45)	DSS (n=15)	P value
Age (years) (mean±SD)	7.05±4.23	8.26±5.18	6.91±4.33	0.425^{ns}
Sex				
Male, n (%)	25 (50.0)	29 (82.4)	7 (54.5)	0.397^{ns}
Female, n (%)	13 (50.0)	16 (17.6)	8 (45.5)	

Note: ns-Non-significant.

Table 3: Distribution of study population as per severity according to history of past symptomatic dengue infection (N=98).

Variables	DF (n=38)	DHF (n=45)	DSS (n=15)	P value
With prior symptomatic infection, n (%)	9 (23.6)	8 (17.7)	2 (13.3)	0.643^{ns}
Without prior symptomatic infection, n (%)	29 (76.3)	37 (82.2)	13 (86.6)	

Note: ns-Non-significant.

Ninety-two patients (93.8%) were treated with isotonic fluid. Only thirty-nine patients were given colloid (39, 36.79%). Patients with DSS were initially treated with isotonic fluids. Colloid was administered to the patients with DSS who`s symptoms of shock were not improved with isotonic fluid replacement. Patients whose hematocrits were decreasing gradually required blood transfusions. One patient with DSS expired in this study due to irreversible shock with multi organ failure. Majority of the patients 79 (80.6%) in this study did not have a past history of documented symptomatic dengue infection. Only 19 patients (19.38%) had past history of documented dengue infection (Figure 1). Here, 9 (23.6%) out of 38 DF patient and 8 (17.7%) out of 45 DHF patient had presented with past symptomatic dengue infection. Among 15 patients with DSS only 2 (13.3%) had previous symptomatic dengue infection. There was no statistically significant ($p>0.05$) difference between DF, DHF and DSS with or without past history of symptomatic dengue infection (Table 3).

DISCUSSION

It can be theoretically postulated that subsequent infection with dengue virus would be more severe than the first episode. WHO also states the same. Contrary to that, in this study we found that only 23.6 percent of patients with dengue fever and 17 % with dengue hemorrhagic fever had history of symptomatic dengue in the past.

Also, our study showed the severity of disease in terms of DF, DHF and DSS did not have significant difference between the groups with or without prior symptomatic infection. One similar study also reported similar findings where 82.1% of study population with Dengue Hemorrhagic fever had no documented previous symptomatic dengue infection.[9]

Our study found age and sex doesn't determine the severity of dengue infection. According to a study conducted in Srilanka sex distribution of dengue patients was similar in males (55.2%) and females 44.8%.[10] But a similar study conducted in a multicenter hospital in Bangladesh suggested variation in presentation across gender with male to female ratio 1.2:1.[11] And another study conducted in India showed equal sex distribution.[12] Khoa et al mentioned age at dengue infection is recognized as playing a key role in characterizing the risk of clinical attack and disease severity and contribution of age in disease development is yet to be quantified.[13]

A study in Thailand stated plasma leakage is a life threatening complication of dengue.[14] In our study huge majority of population with plasma leakage had no prior symptomatic dengue. But another study showed severe plasma leakage was the most common presentation among children.[15] Next study found that dengue patients with BMI more or equal to 25 or those who presented with platelets count <1,00,000/mm^3 or AST or Alt more or equal to 100 on days 3 to 4 are at risk of occurrence of plasma leakage.[1] Dengue in children has varying presentations. Similar to other studies we also found that fever was present in all patients with dengue. Abdominal pain was the second major symptoms followed by vomiting, rash and headache. An Indian study also suggested 100% of study population had fever which was followed by headache, malaise and abdominal pain.[17] Another study conducted in India also reported fever to be the most predominant feature in dengue and abdominal pain being the second one.[18]

Similar study stated a variety of manifestations including that abdominal pain, purpuric, rash, ascites, thrombocytopenia, coagulopathy and raised ALT had a statistically significant predictability for developing DHF.[19] It is difficult to clearly state what determines the severity in subsequent infections. The severity of the dengue infection could be an outcome of multiple factors. The environmental conditions, host's immunological status, genetic factors as well as genetics of the virus may play a role. Connection to T cell Immunity, certain HLA class I and class II loci have been linked to dengue hemorrhagic fever.[20] Secondary infection may be more common in DENV 2 than DENV 1 infections because DENV 2 infections resulted in lower plasma viral RNA

concentrations and viral concentrations were higher in secondary infection.[21] Since the 1960s, numerous reports have identified a second heterologous dengue virus infection as a principal risk factor severe dengue disease(dengue hemorrhagic fever/dengue shock syndrome).[22] A study reported children, aged 3 and 4 years, with DEN-2 infections were found to have high death rate.[23] Socio-economic status, cultural behaviors, climatic changes, and adaptive immunity may also be the determinants.

Limitations

This was a small sample retrospective record based study. So, we recommend further multi-center study with larger sample size to evaluate our finding by considering the all-confounding factors.

CONCLUSION

In our study we noticed that majority of the patients 79 (80.6%) did not have a past history of documented symptomatic dengue infection. There was no increase in dengue morbidity with documented previous symptomatic dengue infection.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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