Clinical Medicine Research
2021; 10(4): 142-150
http://www.sciencepublishinggroup.com/j/cmr
doi: 10.11648/j.cmr.20211004.16
ISSN: 2326-9049 (Print); ISSN: 2326-9057 (Online)

Clinical Presentations, Outcome and Cost of Illness of Dengue in a Tertiary Care Hospital of Bangladesh: An Observational Study

Nur Jahan Aktar[1], Milton Barua[2, *], Amanat Ullah[3], Abdus Sattar[4], Shoman Sarkar[4], Sujat Paul[4], Shofiur Rahman[5], Mitan Chakma[6], Mahmudul Islam Talukder[7], Mahatabur Rahman[8], Mohammad Faisal Kabir[9]

[1]General Medicine, University Hospitals Bristol and Weston NHS Foundation Trust, North Somerset, UK

[2]Department of Medicine, Chittagong General Hospital, Chittagong, Bangladesh

[3]Acute Medicine, Medway NHS Foundation Trust, Kent, UK

[4]Department of Medicine, Chittagong Medical College Hospital, Chittagong, Bangladesh

[5]Department of Cardiology, Chittagong General Hospital, Chittagong, Bangladesh

[6]Department of Otolaryngology, Chittagong Medical College Hospital, Chittagong, Bangladesh

[7]Department of Medicine, Dhaka Medical College Hospital, Dhaka, Bangladesh

[8]Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

[9]Department of Medicine, MH Samorita Hospital & Medical College, Dhaka, Bangladesh

Email address:

dr.miltonbarua@gmail.com (M. Barua)

[*]Corresponding author

To cite this article:

Nur Jahan Aktar, Milton Barua, Amanat Ullah, Abdus Sattar, Shoman Sarkar, Sujat Paul, Shofiur Rahman, Mitan Chakma, Mahmudul Islam Talukder, Mahatabur Rahman, Mohammad Faisal Kabir. Clinical Presentations, Outcome and Cost of Illness of Dengue in a Tertiary Care Hospital of Bangladesh: An Observational Study. *Clinical Medicine Research*. Vol. 10, No. 4, 2021, pp. 142-150.
doi: 10.11648/j.cmr.20211004.16

Received: June 30, 2021; **Accepted**: July 12, 2021; **Published**: August 9, 2021

Abstract: Background: Dengue is a fast-emerging viral disease in many parts of the world, having a potential to present with a varied spectrum of clinical manifestations with atypical presentations being more frequent. This study was conducted to evaluate the clinical features, outcome and Cost of Illness (COI) of dengue cases admitted in a tertiary-care government hospital in Chattogram, Bangladesh. Methods & materials: It was a hospital based prospective observational study and was carried out in the Department of Medicine, Chittagong Medical College Hospital. All the consecutive serologically positive (NS1 antigen, IgM, IgG antibodies) dengue cases (age >12 years) admitted in the Department of Medicine of Chittagong Medical College Hospital from 1st August 2019 to 31st July 2020, were enrolled in the study. Severity of each dengue case was determined as per the recent WHO classification (2009) Clinical presentations of the cases were carefully assessed. In-hospital outcomes of the patients in terms of mortality, duration of hospital stay, need for ICU or other support were recorded. The COI questionnaire included three major cost components: direct medical costs (DMC), direct non-xiv medical costs (DNMC), and indirect costs (IC). Data analysis was done on the SPSS 23 version. Results: Out of 425 patients, the maximum number of dengue cases reported were males (76.9%) and belonging to the 21-30 years age group (38.8%). Fever was the main complaint in all the cases followed by headache (78%), myalgia (56%), persistent vomiting (44%). Of the 91.5% Dengue fever cases, 88.2% were classified as Dengue fever without warning signs and 3.3% with warning signs and 8.5% as severe dengue. Thrombocytopenia was present in 53.9% and leukopenia in 42.1% of cases. 3.3% of patients needed ICU admission and the mortality rate was 1.2%. The median total COI was BDT 8703 (IQR: 6240-11795) with median DMC of 3580 (IQR: 2525-4885), DNMC of 2000 (IQR: 1250-3225) and INMC of 2400 (IQR: 1045-4000). Conclusions: Overwhelming number of cases and their varied clinical presentations lead to an increase in hospitalization in this outbreak. Though the outcomes have been mostly favorable, the cost incurred as a result has been immense and has impacted households greatly, since most medical costs in Bangladesh are out-of-pocket expenses.

Keywords: Dengue Fever, Clinical Presentations, Outcome of Dengue, Cost of Illness (COI)

1. Introduction

Dengue fever is an acute febrile viral disease transmitted by the bite of aedes mosquitoes carrying any one of the four dengue viral serotypes. Approximately half of the world's population is at risk, especially people residing in tropical and subtropical climates such as in Bangladesh. About 390 million dengue infections are estimated to occur annually, of which a quarter of the cases (67–136 million) would manifest clinically [1], with the overall incidence of dengue having increased 30-fold over the past 50 years [2]. At least 164 people died of Dengue fever across Bangladesh in 2019. According to the latest figure reported by the Directorate General of Health Services (DGHS), the deaths included 2 in April, 6 in June, 35 in July, 83 in August, 25 in September, 11 in October and 2 in November [3]. The reported dengue cases reached 101,354 in 2019, when the number of dengue fever (DF) patients was only 10,148 in 2018 with 26 deaths [4]. Though the outbreak of DF is continuing in similar fashion every year, interestingly the typical presentation of DF has changed and it is of concern, as identifying the atypical presentation is challenging and may lead to increased mortality. And to highlight this shift in paradigm of clinical presentation, Expert consensus groups in Latin America (Havana, Cuba, 2007), South-East Asia (Kuala Lumpur, Malaysia, 2007), and at WHO headquarters in Geneva, Switzerland in 2008 agreed that: "Dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome" [5]. To demonstrate this, a study reviewed 40 Dengue cases from January to December 2016 in Dhaka Medical College Hospital and reported that arthralgia and retro-orbital pain were the most common clinical features in their dengue cases instead of headache and rash with fever [6]. But in another study, most common symptoms after fever were headache, abdominal pain and myalgia [7]. So clearly it is evident that dengue presents in a very non-uniform manner making it very concerning. The local drivers of dengue activity in Bangladesh are poorly defined. It was observed that Dhaka was the worst hit whenever an outbreak took place but there has been a similar picture in other regions as well, though to a lesser degree. Mahmood and colleague (2011) suggested that several macro-level risk factors including over-population, uncontrolled urbanization, and poor waste management had played prominent roles in the emergence of dengue in Bangladesh [8]. To estimate the burden of any disease, the cost of illness (COI) is an important primary source of data. However, in a system where out-of-pocket expenses are the major source of payments for health, keeping track of escalating COI can be challenging. Nevertheless, quite a few studies have been conducted in different countries of the world with this regard. One study performed in India from 2006 to 2012 reported that the average cost of a hospitalized case of dengue was about USD 235 [9]. The median and interquartile range (IQR) direct costs for adult dengue without warning signs, dengue with warning signs, and severe dengue were USD 312.75, USD 287.22, and USD 720.39, respectively [10], thus coming to the conclusion that dengue infection was definitely a financially crippling disease. Several other studies have been conducted to estimate the economic burden of DF in a multi-country setting based on primary data sources using standardized methods [11, 12]. There is no doubt that all of the existing studies have contributed to informing the importance of the economic burden of DF, but it is also true that more studies are essential to better understand the economic impact of DF in many of known and unknown dengue-endemic countries. Understanding the accurate economic set back caused by a disease is one of the most important steps in grasping a full scope of preventive programs which would benefit the society as it was reported that, an estimated 55 million Indians were pushed into poverty by healthcare costs every year [13]. Moreover, the range of the total COI for DF also plays a critical role in determining the threshold costs for which dengue vaccination would be effective [14]. COI is rarely done in Bangladesh but is an essential component of understanding the devastating effect of an illness and supporting the planning of health services and policy. So, to contribute to the sparse literature on the economic burden of dengue, the present study was aimed to assess the COI of DF in addition to assessing the presentations and outcome of cases in Chittagong Medical College Hospital (CMCH) in Chattogram, Bangladesh.

2. Materials and Methods

After getting approval from the Ethical and Review Committee of CMC, this hospital based observational study was conducted in the Medicine Ward of the CMCH from 1st August 2019 to 31st July 2020. All the admitted patients were invited to take part in the study voluntarily. After obtaining informed consent, data was collected by face to face interview of the respondents with the help of a pretested semi-structured interview schedule. Dengue serology (Rapid qualitative immune-chromatographic test NS1 antigen was done in patients who presented with fever for 3 days or of lesser duration and Dengue IgM and IgG was done in those who come with fever for more than 5 days. All adult dengue patients (age >12 years) of both sexes with positive serological tests (either done at the hospital or prior to being admitted in the hospital) were included consecutively in the study. Patients who refused to participate in the study were excluded. The cases were classified according to WHO Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Hemorrhagic fever, 2011 [15]. The variables recorded were demographic profile, clinical manifestations, laboratory parameters (complete blood count (CBC) including white blood cell count (WBC) and platelet

count), outcome and cost of illness (COI) and recorded on a pretested interview-administered pre designed semi structured questionnaire.

Dengue without warning sign was defined when fever and two of the followings (Nausea, vomiting, Rash, Aches and pains, Leukopenia, Positive tourniquet test) were present. Dengue with warning signs was defined as above with any of the following: Abdominal pain or tenderness, Persistent vomiting, Clinical fluid accumulation (ascites, pleural effusion), Bleeding: Epistaxis, black stool, hematemesis, excessive menstrual bleeding, dark colored urine (hemoglobinuria) or hematuria, Lethargy, restlessness, Giddiness. Pale, cold and clammy hands and feet, Less/no urine output for 4– 6 hours Liver enlargement > 2 cm, Laboratory: Hematocrit>20% concurrent with rapid decrease in platelet count.

Dengue fever (DF) was defined as presence of fever and two or more of the following, retro-orbital or ocular pain, headache, rash, myalgia, arthralgia, leukopenia, or hemorrhagic manifestations (e.g. positive tourniquet test, petechiae; purpura/ecchymosis; epistaxis; gum bleeding; blood in vomitus, urine, or stool; or vaginal bleeding) but not meeting the case definition of dengue hemorrhagic fever. Anorexia, nausea, abdominal pain, and persistent vomiting may also occur but are not case-defining criteria for DF. Dengue hemorrhagic fever (DHF) was defined as Fever lasting from 2-7 days, evidence of hemorrhagic manifestation or a positive tourniquet test, thrombocytopenia (≤100, 000 cells per mm^3), evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit ≥ 20% above average for age or a decrease in hematocrit ≥ 20% of baseline following fluid replacement therapy), or pleural effusion, or ascites or hypoproteinemia. Dengue shock syndrome (DSS) is defined as all criteria for DHF plus circulatory failure as evidenced by: rapid and weak pulse and narrow pulse pressure (>20 mm Hg) or age specific hypotension and cold, clammy skin and restlessness.

A positive IgM and negative IgG is indicative of primary dengue infection and a positive IgG with or without a positive IgM is indicative of active secondary infection. Thrombocytopenia was defined as total platelet count of 100,000 cells or less per cu.mm. Leucopenia was defined as WBC count less than 4000 cells per cu.mm.

Cost of Illness (COI): This survey included three major cost components: direct medical costs (DMC), direct non-medical costs (DNMC), and indirect costs (IC). DMC: consisted of consultation fees outside hospital (prior admission), medication, laboratory tests, and all other costs which were directly related to the medical treatment of the dengue illness. Patients were asked how much money they had spent for medical services that they received, and whether they had to bear all of the expenditure directly or was it covered by any external supports such as private/public insurance, loans from family or friends, government subsidies, or non-governmental aids. In order to capture the full spectrum of the DMC, hospital/medical/investigation bill records were also accessed to understand how the DMC burden was distributed. DNMC: Included all expenditure spent for food, lodging, and transportation for a patient as well as the patient's accompanies. IC: Took into account the costs of productivity loss (i.e. wage loss, missing school days) by patients and substitute laborers, and caretakers. In order to estimate productivity loss, the self-reported daily wage loss was asked for patients who made earnings. For students who did not earn any wages, the yearly government expenditure per student as per UNESCO-2016 data for secondary education (PPP$ 365.38) and tertiary education (PPP$ 1105.48) was used to convert their productivity loss into monetary value [16]. If the patient was neither a wage-worker nor a student (i.e. unpaid housework), the minimum wage of the country (BDT 8000) was applied. While the government expenditure per primary student is useful for estimating average spending on one student, the use of this indicator may underestimate their productivity loss as the indicator does not include household contributions. In addition to productivity loss, patients were also asked whether they have hired any substitute laborers or caretakers during their illness. If yes, a series of questions related to the duration and payments of having substitute laborers and/or caretakers was asked. In case that patients did not pay anything for having them (i.e. household members), the opportunity costs of substitute laborers/caretakers were estimated by taking into account the daily payments for doing their usual activities which they would have done otherwise. It should be noted that the questionnaire was carefully designed in order to avoid any duplication of the costs.

In hospital outcome: Only immediate or short outcomes were observed as outcome of the disease which encompassed total duration of hospital stay, clinical improvement, referral to ICU, development of complications or mortality outcome during the hospital course.

After collection, data was entered into Microsoft Excel data sheet to produce a master sheet. Then they were fed into SPSS (Statistical Package for Social Science) for Windows version 23 software for the processing and analysis. Continuous variables were reported as means and standard deviation and categorical variables were reported as count and percentages. Between groups comparisons were done either by Chi square test or Fisher exact test for categorical data. Statistical significance was defined as $P<0.05$ and confidence interval set at 95% level.

3. Results

Table 1 shows that, rural representation was more than urban are (55.8% versus 44.2% respectively). Majority of the patients were Muslim and having educational qualification either primary or secondary level.

Table 2 shows that, majority of the patients (89.4%) had no associated co morbidity or any risk factors for developing severe dengue. Only 5 patients reported to take NSAIDs for their current illness and 2 patients were on anticoagulant for previous conditions.

Table 3 shows that, most prominent waring sign was persistent vomiting present in 65 (15.3%) of cases. Other common warning signs were severe abdominal pain (63%),

bleeding (31%) and giddiness (24%).

Out of 425 dengue cases, majority of the cases (92.2%) showed NS1Ag positivity. IgM anti-dengue antibody were found positive in 59 (13.9%) samples, IgG antibody were positive in 44 (10.4%) and both IgM and IgG were positive in 27 (6.4%) samples (Table 4).

Table 1. *Socio-economic characteristics of the dengue patients (n=425).*

Variables	Level	Frequency (percentage)
Residence	Urban	188 (44.2)
	Rural	237 (55.8)
Religion	Muslim	349 (82.1)
	Sonaton	61 (14.4)
	Buddhist	15 (3.5)
Education	Illiterate	24 (5.6)
	Primary	129 (30.4)
	Secondary	149 (35.1)
	Higher secondary	71 (16.7)
	Graduate &above	52 (12.2)
Marital status	Unmarried	208 (48.9)
	Married	207 (48.7)
	Divorced/widowed	8 (2.4)
Monthly family income	Median (IQR), in BDT	15000 (10000-25000)

IQR: Interquartile range; BDT: Bangladeshi taka.

Table 2. *Comorbidity status and drug history of the dengue patients (n=425).*

Variables	Level	Frequency (percentage)
Comorbidity &risk factors	Absent	380 (89.4)
	Present	45 (10.6)
Drug history	None	396 (93.6)
	NSAIDs	5 (1.2)
	Anticoagulant	2 (0.5)
	Paracetamol	14 (3.3)
	Others	6 (1.4)

Table 3. *Warning signs at presentation in dengue cases (n=425).*

Warning signs (symptoms/ signs)	Frequency (percentage)*
Persistent vomiting	65 (15.3)
Severe abdominal pain/tenderness	63 (14.8)
Bleeding (epistaxis, gum bleed, hematemesis, menstrual, haematuria)	31 (7.3)
Giddiness	24 (5.6)
Pale, cold and clammy hands and feet	14 (3.3)
Less/no urine output for 4-6 hrs.	13 (3.1)
Lethargy /restlessness/sudden behavioral change	12 (2.8)
Clinical fluid accumulation	5 (1.2)
Liver enlargement >2 cm	4 (0.9)

*Includes multiple response.

Table 4. *Distribution of cases according to dengue rapid test positivity (n=425).*

Rapid test results	Frequency (percentage)
NS1 Ag +	392 (92.2)
Dengue Ig M Ab +	59 (13.9)
Dengue Ig G Ab +	44 (10.4)
Both Ig M Ab &Ig G Ab +	27 (6.4)

Table 5. *Laboratory findings of the dengue cases (n=425).*

Parameters	Levels	Frequency (%)
Total leucocyte count	Leucopenia (<4000cells/mm)	179 (42.1)
	Normal	242 (56.9)
	Increased	4 (1)
Platelet count	≤ 50000	106 (24.9)
	50000-1 lakh	145 (34.1)
	≤ 1 lakh	240 (56.5)
Hematocrit (%)	Mean (SD)	39.48 (5.02)
	Range	21-54

Laboratory test results are presented in Table 5. More than half of the cases had moderate or severe thrombocytopenia and about 42.1% of cases had leucopenia, but only 1% had leukocytosis.

Majority of the cases (88.2%) included in the study were classified as DF without any warning sign followed by DF with warning sign in 14 (3.3%) cases. Thirty-four (8%) of the patients were classified as DHF. Only 2 cases were classified as Expanded dengue syndrome.

Table 6. *Final diagnosis of the dengue cases (n=425).*

Type	Level	Frequency (%)
Dengue fever	Without warning sign	375 (88.2)
	With warning sign	14 (3.3)
Dengue hemorrhagic fever	Without shock	19 (4.5)
	With shock or DSS	15 (3.5)
Expanded dengue syndrome		2 (0.5)

Table 7. *Outcome of the dengue cases (n=425).*

Outcome	Frequency (percentage)
Improved and discharged	404 (95.0)
Referred to ICU	14 (3.3)
Referred to CCU	2 (0.5)
Died	5 (1.2)

The outcome of the dengue cases in the study is shown in table 7. It depicts that, 404 (95%) cases improved clinically and were discharged in stable condition. Five cases died (1.2%) during the course of treatment and 14 cases needed ICU, mostly due to DSS and 2 CCU referrals with acute myocardial infarction and myocarditis.

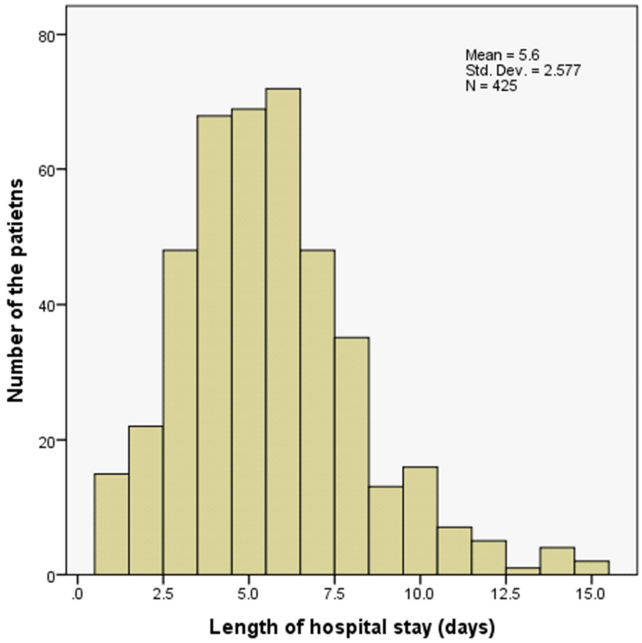

Figure 1. *Histogram showing the distribution of length of hospital stay of the dengue cases.*

Figure 1 shows that, duration of hospital stay ranged from 1-15 days with a mean duration of 5.5 days.

Table 8. *Cost of illness of the dengue cases by disease severity (n=425).*

Cost category	DF (n=402)	DHF (n=21)	All (n=425)
Direct cost	5820 (4825-7781)	7624 (4570-14677)	5830 (4295-7904)
Medical cost	3522 (2520-4732)	4994 (3214-10805)	3580 (2525-4885)
Non- medical cost	2000 (1250-3200)	2590 (1100-4475)	2000 (1250-3225)
Indirect cost	2400 (1000-4000)	2500 (2100-3500)	2400 (1045-4000)
Total cost	8600 (6207-11450)	11226 (6242-20677)	8703 (6240-11795)

All costs are reported in Bangladeshi taka and in Median (interquartile range).

Table 8 presents the direct, indirect and total costs of hospitalized dengue cases to households by patient disease severity. The median total cost of a hospitalized dengue case was BDT 8703 (IQR: 6240-11795). The direct costs amounted to BDT 5830 (IQR: 4295-7904), constituting 71% of the total costs while the median indirect cost was BDT 2400 (IQR: 1045-4000). Overall, the total household cost of a hospitalized dengue case increased with disease severity. The direct medical costs and the indirect costs were notably higher for DHF cases compared to DF cases.

4. Discussions

This was a prospective clinico-epidemiological and cost-of-illness study, which aimed to determine the clinico-epidemiological features of dengue cases and quantify the direct, indirect and total costs of hospitalized dengue cases during a dengue epidemic in Chattogram city of Bangladesh. A total of 425 admitted dengue cases were included in the study from the adult medicine ward of CMCH from August 2019 to July 2020. In the present study, more than two third of dengue patients were below 30 years of age. This is consistent with other studies done locally as well as in other dengue endemic countries like Pakistan, India and Malaysia [17-21]. Decades ago, DF was typically acknowledged to be a disease of early childhood, while clinical DF in adults was rare. DHF/DSS in these areas occurred mostly in children aged 2-15 years. Older and many of the younger inhabitants were usually immune and escaped DHF, as they would have acquired immunity against primary infection [22]. However, the present study and other recent studies demonstrated an increase of dengue incidence in older age groups. The mean (SD) age of the dengue cases in the present study is 28.94 (12.52) years. Singh et al., (2017) from India also reported maximum cases in the age group 21-30 years with a mean age of 32.26 (12.04) years [23]. This age group is the most active population of the society who are mostly working class, indicating more transmission of dengue infections at work

sites. A similar finding was observed in a study done in Central India [24]. The impact of affecting this age group is paramount and is proportional to the financial loss incurred, as this is the major contributor of our economy being the 2nd largest working age population [25]. In the current study, the male to female ratio is 3.34: 1. There are many studies from the South-East Asia region that suggest a higher ratio of males than females in DF/DHF hospitalized cases (Bangladesh, India, Malaysia and Saudi Arabia), and only few studies suggest no difference in sexes [17, 20, 21, 26]. It is to be noted that, almost all of these studies including the present one was hospital-based, thus, probably only represent those who had access to healthcare rather than the infected population. Nevertheless, males are more affected than females probably due to more outdoor activity than the females. Other reasons of male predominance might be working adults, who are mostly males, would seek medical attention from a hospital as they require medical certification to be excused from work. In addition, they are probably the only earning member of the family and thus get more attention from other members of the family to seek medical care. However, this difference may not indicate more susceptibility of males to dengue infection, because females in these areas are less privileged and do not get equal opportunity of being treated in a hospital for fever. This trend is obvious as in 2000 outbreak, there was no significant difference in sex among dengue cases in Dhaka Bangladesh [18]. Though urbanization is considered to be an important factor for the dengue epidemic, in the present study, representation from rural areas was more than urban area (55.8% versus 44.2%). In some countries, incidence of dengue is higher in rural areas than in urban areas [1]. The change in trend could be because of various reasons. It was observed during the study that there was extensive travel and mobilization of people from rural to urban areas which is consistent with the study by Zafar et al., 2010 [28]. Furthermore, rural areas are peri-urbanized with high population density as 63% of our total population is from rural areas [29]. The disease was more frequent among those with secondary or low educational levels. This finding was in accordance with a Saudi study where the majority of the cases had education up to secondary school or below [27]. As we have the largest number of pupils enrolled in primary and secondary education [29], this finding was not surprising owing to their lack of awareness about the disease. Majority of the cases in the present study were Muslims with a median monthly family income of BDT 15000. According to our national data and the study site which was a government tertiary care hospital and thus these findings were expected.

In the present study, fever was the main complaint in all the cases of dengue reported in the hospital. Other most frequent symptoms were headache (78%), myalgia (56%) and vomiting (44%). An earlier study from Bangladesh reported that the most frequent features were: high fever (100%), severe headache (80%), external bleeding (79%), severe body ache (64%), red eye (56%), eye ache (34%), altered bowel (33%), cough (30%), and abdominal pain (26%) [17]. In the present study rashes were seen in only 15% of cases. Findings of the present study were similar with the study done recently around our country 23, 30, 31]. One thing is to be noted that, external bleeding and bleeding manifestations were infrequently noticed in the present cohort. In contrast Yunus et al., (2001) reported a higher frequency of these events like positive Tourniquet test in 60%, cutaneous bleeding in 64%, and hemorrhage in 79% [17]. In the present study only bleeding manifestations were reported by only 7.3% cases which were mostly mucosal. Tourniquet test was not done due the painful nature of the procedure and that could point towards the lower incidence of evidence of bleeding. Furthermore, diarrhoea was seen in 13% of the cases which was an unusual presentation in adults in this study as it was not a common presentation previously in Bangladesh. It was significant in children with 23% having diarrhea symptoms during the 2000 outbreak in Chattogram [32]. Interestingly, diarrhoea was one of the predominating symptoms found in a study conducted in Singapore 33], but not seen elsewhere such as Bangladesh, France, India, Thailand, Taiwan, Sri Lanka and Pakistan [34]. The different predominant circulating serotypes of dengue virus in different locations could possibly explain the differences in the frequency of diarrhea 33, 35]. Perhaps, a more complex virus and host interaction could be the underlying pathogenesis for the occurrence of diarrhoea. Seet et al. explained that diarrhoea could increase vascular leakage and lead to osmotic diarrhea [33]. As diarrhoea is not included in the list of warning signs by WHO, we should, therefore, be vigilant about patients who present with diarrhoea, as some of them were seen to have unfavorable outcomes. These results indicate the changes in the clinical presentation of dengue fever patients in the current time.

All the 425 cases included in the study were serologically confirmed dengue cases with either NS1 antigen or antibody positivity. Almost 92.2% of cases showed NS1Ag positivity. IgM anti-dengue antibodies were found positive in 59 (13.9%) samples, IgG antibodies were positive in 44 (10.4%) and both IgM and IgG were positive in 27 (6.4%) samples. These findings were consistent with the findings of Singh et al., (2017) [23]. Thrombocytopenia (56.5%) was the most common laboratory finding of dengue fever followed by leukopenia (42.1%) similar to the study done by Singh et al., (2017) [23]. Platelet count of below 50,000 and 50,000-100,000 was seen in around 24.9% and 34.1% respectively in the present study. Thrombocytopenia is an important laboratory parameter for assessment of dengue severity and also in differentiating it from Chikungunya where thrombocytopenia is not as common, especially when there is no serological confirmation of the cases [36]. Dengue fever represented 91.5% cases, Dengue Hemorrhagic Fever 8% and there were only 15 (3.5%) cases of Dengue Shock Syndrome reported during the present study period. There were only 2 cases classified as Expanded Dengue Syndrome. Rahman et al., (2002) also reported that dengue fever occurred most commonly (60.20%), followed by dengue hemorrhagic fever (39.20%) and dengue shock syndrome (0.60%) [26]. Singh et al., (2017) observed that, in India in the year 2015 the percentage of severe dengue cases were comparatively lower than the year 2010 [23]. In the present

study the majority (95%) of the cases improved clinically and were discharged in stable condition. Only five deaths occurred in the reported dengue cases in this study giving a case fatality ratio of 1.2% and these deaths were due to DSS. Almost all of the cases of death, had presented late, during the course of their illness, for treatment. Such an unfortunate outcome could have been prevented with early identification of warning signs and disease severity and prompt management at the point of first contact with health care facilities by the patients. Recent studies from India [23] and Pakistan [31] reported similar low mortality (1.25% and 0% respectively). The overall mortality of dengue infection is thus low if treated appropriately and promptly, however the mortality associated with DHF and DSS is high as these patients need platelets transfusion, ICU settings and ventilator support which is scarce in designated health care facilities. Majority of the dengue cases had stayed for 6 days or less in hospital in the present study. As most of the cases in the study were DF with or without warning signs the hospital stays were also short. Patients with DSS and Expanded Dengue Syndrome had to stay in the hospital for a relatively longer period as they needed complex supportive care. Similar pattern of hospital stay was also reported by Singh et al., (2017) [23].

To demonstrate the financial burden of the disease, COI was evaluated keeping in mind the fact that we have a system where private healthcare is preferred over government services and out-of-pocket expenses are the major source of payments for health problems. And the present study demonstrated that the median total cost of a hospitalized dengue case was BDT 8703 (IQR: 6240-11795). The direct costs amounted to BDT 5830 (IQR: 4295-7904), constituting 71% of the total costs while the median indirect cost was BDT 2400 (IQR: 1045-4000) which was mainly the transportation that added up the cost. While collecting data it was observed that majority of the patients had sought some sort of medical consultation, mostly from private practitioners, prior to admission and would have carried out a significant number of investigations including dengue serological tests which had incurred a huge direct medical cost that is seen here despite the fact that the study was done in a government hospital, where most of the medical services are for free. This financial burden on the individuals could be overcome, if the service in the government health care system is upgraded to increase the capacity and quality, especially the laboratory facilities, by giving enhanced services, which would make the government sector as alluring as the private health care facilities. This, of course, needs autonomy in financial capacity to mitigate the problem and requires attention of the policy makers. Overall, the total household cost of a hospitalized dengue case increased with disease severity as the patients needed ICU support or had to stay longer in hospital. The direct medical costs and the indirect costs were notably higher for DHF cases compared to DF cases. To our knowledge, there was no study on COI for dengue in Bangladesh. However, though limited, there is data on COI in India and Thailand. Tozan et al., (2017) reported that, the total cost of hospitalized dengue cases in semi-rural areas of Thailand was USD 171.2 and USD 226.1 for adult DF and DHF patients, respectively [37]. Panmei et al., (2019) from India reported that, the median and IQR direct costs for adult dengue without warning signs, dengue with warning signs, and severe dengue were USD 312.75 (IQR 174.55–531.03), USD 287.22 (IQR 210.96–389.34), and USD 720.39 (IQR 389.23–1035.51), respectively [10]. These studies also highlight the high cost incurred by the illness, though the amount is much higher when compared to our data where total cost (BDT 8703) is estimated to be USD 102.62 at current exchange rate [38]. It is important to note that the type of patients generally varies from place to place in terms of their cultural, rural/urban setting, ethnic backgrounds, health care system and their financial capability. In spite of these differences, all the previous studies point towards the financial burden of the disease. As per the national survey done in 2016, the average monthly income per household was BDT 15945 at national level with an average income of BDT 16073 in Chattogram Division. The per capita monthly income was only BDT 3936 [39] and as per our data, the median monthly household income is BDT 15000 which is slightly lower than the statistical data available to us. The total cost of hospitalization which is BDT 8703 thus represents about 42% of the total household income estimated by us, which is staggeringly higher than the data available on allocated average monthly household medical expenditure, i.e. 4.54% [39]. This reflects how dengue is paralyzing patients and their families and urgently calls for a nation-wide study to accurately assess the overall economic devastation created by dengue on households. As the place of study was a tertiary care hospital in the city of Chattogram, most of the patients were from Chattogram district (360). There were cases from other districts too like Bandarban (18) and Cox's Bazar (11). In Chattogram district, Kotwali thana had the greatest number of cases (11.38%) followed by Boalkhali (10.27%) and Biswa Colony of Akbar Shah (9.44%). In our extensive literature review, we had failed to find a study indicating previous hotspots of dengue in Chattogram and thus could not compare my findings.

5. Limitations

This study had some limitations. This study was conducted by consecutive sampling from one government level tertiary care hospital. This study assessed the cost of a dengue febrile illness only for the hospitalized cases, not for the community level. Direct Medical cost only included the cost of diagnosis and treatment and not prevention. Follow-up study of the cases after discharge was not possible.

6. Conclusions

In conclusion, the incidence of dengue was more in male, the peak age group being 21 to 30 years. Fever with headache, pain (myalgia, retro orbital pain) and persistent vomiting were the main clinical presentations found in adults with dengue. Most of the dengue cases were DF with a case fatality rate of 1.2%. The total cost of hospitalized dengue cases accounted for about 42% of the monthly household income. High

household costs of dengue illness strongly justify efforts to improve the coverage of preventive and control measures against dengue. In addition, improving management by identifying early warning signs at peripheral centers would likely reduce the burden on the tertiary hospitals and the patients, where cost of care is higher. Emphasis should also be given on improving the capacity of government hospitals in terms of diagnostic facilities and empowering local hospitals with the financial capacity to ensure implementing these changes.

References

[1] Bhatt, S., Gething, P., Brady, O., Messina, J., Farlow, A., Moyes, C., Drake, J., Brownstein, J., Hoen, A., Sankoh, O., Myers, M., George, D., Jaenisch, T., Wint, G., Simmons, C., Scott, T., Farrar, J. and Hay, S., 2013. The global distribution and burden of dengue. Nature, 496 (7446), pp. 504-507.

[2] World Health Organization. (2019). What is dengue? [online] Available at: https://www.who.int/denguecontrol/disease/en/ [Accessed 21 Aug. 2019].

[3] DGHS (Directorate General of Health Services). Health Bulletin on current Dengue situation published by CDC, DGHS. [Internet]Available from: https://reliefweb.int/report/bangladesh/bangladesh-dengue-situation-2019-healthbulletin-volume-2-03-august-2019.

[4] Dghs.gov.bd. 2020. Daily Dengue Status Report. [online] Available at: https://dghs.gov.bd [Accessed 5 September 2020].

[5] World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. Geneva: World Health Organization Press; 2009.

[6] Pervin, M., Sweety, A., Hossain, M., Sharmin, R., Fatema, N., Rahman, M., Nehar, N., Yasmin, M., Khoda, M., Rahman, K. and Azad, K. (2018). Seraepidemiology of Dengue Virus Infection in Clinically Suspected Patients Attended in Dhaka Medical College Hospital During January to December 2016. Journal of Dhaka Medical College, 26 (2), pp. 111-116.

[7] kumar, M., Verma, R. and Kumar, D. (2019). Recent Trends in Clinical Presentation in Cases of Dengue Presenting At Tertiary Care Hospital. International Journal of Science and Healthcare Research, 4 (1), pp 507-509.

[8] Mahmood B, Mahmood S (2011) Emergence of dengue in Bangladesh a major international public health concern in recent years. J. Environ. Res. Manage. 2 (3): pp. 35–41.

[9] Shepard, D. S., Halasa, Y. A., Tyagi, B. K., Adhish, S. V., Nandan, D., Karthiga, K. S., et al. (2014) Economic and disease burden of dengue illness in India. Am J Trop Med Hyg, 91 (6): pp. 1235–42, doi: http://dx.doi.org/10.4269/ajtmh.14-0002.

[10] Panmei, K., Joseph, A., Rose, W., Abraham, O., Mathuram, A., Kumar, S. and Abraham, A. (2019). Direct cost of illness for dengue in hospitalized children and adults at a referral hospital in India. International Journal of Infectious Diseases, 84, S64-S67.

[11] Suaya, J., Lum, L., Huy, R., Tyo, K., Sughayyar, R., Armien, B., et al. (2009). Cost of Dengue Cases in Eight Countries in the Americas and Asia: A Prospective Study. The American Journal of Tropical Medicine and Hygiene, 80 (5), pp. 846-855.

[12] Lee J-S, Mogasale V, Lim JK, Ly S, Lee KS, Sorn S, et al. (2019) A multi-country study of the economic burden of dengue fever based on patient-specific field surveys in Burkina Faso, Kenya, and Cambodia. PLoSNegl Trop Dis 13 (2): e0007164. https://doi.org/10.1371/journal. pntd.0007164.

[13] Selvaraj, S., Farooqui, H., & Karan, A. (2018). Quantifying the financial burden of households' out-of-pocket payments on medicines in India: a repeated cross sectional analysis of National Sample Survey data, 1994–2014. BMJ Open, 8 (5), e018020.

[14] Lee, J., Lourenço, J., Gupta, S. and Farlow, A. (2018). A multi-country study of dengue vaccination strategies with Dengvaxia and a future vaccine candidate in three dengue-endemic countries: Vietnam, Thailand, and Colombia. Vaccine, 36 (17), pp. 2346-2355.

[15] World Health Organization. 2011, Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded edition.[Internet] http://apps.searo.who.int/pds_docs/B4751.pdf.

[16] Uis.unesco.org. 2016. Bangladesh | UNESCO UIS. [online].

[17] Yunus, Emran Bin, Bangali, A Mannan, Mahmood, M Ataul Haq, Rahman, M Mushfiqur, Chowdhury, A R. et al. (2001). Dengue Outbreak 2000 in Bangladesh: From Speculation to Reality and Exercises. WHO Regional Office for South-East Asia. https://apps.who.int/iris/handle/10665/163630.

[18] Pervin M, Tabassum S, Ali MM, Mamun KZ and Islam MN. Clinical and Laboratory Observations associated with the 2000 Dengue Outbreak in Dhaka, Bangladesh. Dengue Bulletin. 2004; 28: pp. 96-106.

[19] Raza, F. A., Rehman, S. ur, Khalid, R., Ahmad, J., Ashraf, S., Iqbal, M., & Hasnain, S. (2014). Demographic and Clinico-Epidemiological Features of Dengue Fever in Faisalabad, Pakistan. PLoS ONE, 9 (3), e89868. doi: 10.1371/journal.pone.0089868.

[20] Thaher, M. A., Ahmad, S. R, & Chandrasekhar, A. (2016) Clinical presentation and outcome of dengue cases in a tertiary-care hospital, Hyderabad. Int J Med Sci Public Health, 5 (10), pp. 2009-2012.

[21] Chew, M., Rahman, M. and Salleh, S., 2012. Dengue in Malaysia: An epidemiological perspective study. Pak J Med Sci, 28 (4), pp. 643-647.

[22] Libraty, D. H., Young, P. R., Pickering, D., Endy, T. P., Kalayanarooj, S., Green, S., et al. (2002). High circulating levels of the dengue virus nonstructural protein NS1 early in dengue illness correlate with the development of dengue haemorrhagic fever. J Infect Dis, 186 (6), pp. 1165-8.

[23] Singh, P., Bano, M., Rawat, V., Joshi, A. (2017). Clinico-epidemiological study of Dengue outbreaks- an overview from Kumaon region of Uttarakhand, JMSCR, 5 (4), pp. 20962-20971.

[24] Ukey, P., Bondade, S., Paunipagar, P., Powar, R., & Akulwar, S. (2010). Study of seroprevalence of dengue Fever in central India. Indian journal of community medicine: official publication of Indian Association of Preventive & Social Medicine, 35 (4), pp. 517–519.

[25] Bbs.portal.gov.bd. 2020. 2020. Bangladesh Statistics 2019. [online] Available at: https://bbs.portal.gov.bd [Accessed 3 September 2020].

[26] Rahman, M., ahman, K., Siddque, A. K., Shoma, S., Kamal, A. H., Ali, K. S., Nisaluk, A., & Breiman, R. F. (2002). First outbreak of dengue hemorrhagic fever, Bangladesh. Emerging infectious diseases, 8 (7), 738–740. https://doi.org/10.3201/eid0807.010398.

[27] El-Gilany, A., Eldeib, A. and Hammad, S. (2010). Clinico–epidemiological features of dengue fever in Saudi Arabia. Asian Pacific Journal of Tropical Medicine, 3 (3), pp. 220-223.

[28] Zafar, H., Dhodhy, M., Hayyat, A., Akhtar, N., Rizwan, F., Chaudhary, B. and Zareef, S., 2010. Seroprevalence of Dengue Viral Infection in Healthy Population residing in Rural Areas of District Rawalpindi. International Journal of Pathology, 8 (1), pp. 13-15.

[29] Uis.unesco.org. 2020. Bangladesh | UNESCO UIS. [online] Available at: http://uis.unesco.org/en/country/bd?theme=education-and-literacy [Accessed 3 September 2020].

[30] Md Khaja M, Devadas S. (2017). Clinical profile and outcome of dengue fever in a paediatric tertiary care centre. Int J Contemp Pediatr, 4, pp 875-7. DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20171689.

[31] Hasan S, Jamdar SF, Alalowi M, Al Ageel Al, Beaiji SM. (2016). Dengue virus: A global human threat: Review of literature. J Int Soc Prevent Communit Dent 2016; 6: 1-6. DOI: 10.4103/2231-0762.175416.

[32] Ahmed, F., Mahmood, C., Sharma, J., Hoque, S., Zaman, R. and Hasan, M., 2001. Dengue and Dengue Haemorrhagic Fever in Children During the 2000 Outbreak in Chittagong, Bangladesh. Dengue Bulletin, Vol 25, pp. 33-39.

[33] Seet, R., Ooi, E., Wong, H. and Paton, N., 2005. An outbreak of primary dengue infection among migrant Chinese workers in Singapore characterized by prominent gastrointestinal symptoms and a high proportion of symptomatic cases. Journal of Clinical Virology, [online] 33 (4), pp. 336-340.

[34] Kuan, G., Hin, Y. and Isa, R., 2015. Comparison of vomiting and diarrhoea frequency among dengue-infected patients. Journal of Coastal Life Medicine, 3 (8), pp. 616-620.

[35] Endy TP, Chunsuttiwat S, Nisalak A, Libraty DH, Green S, Rothman AL, et al. (2002). Epidemiology of inappropriate and symptomatic acute dengue virus infection: a prospective study of primary school children in Kamphaeng Phet, Thailand. Am J Epidemiol; 156 (1): pp. 40-51.

[36] National Guideline for Clinical Management of Dengue Syndrome. 2018, National Malaria Elimination & Aedes Transmitted Disease Control Program Disease Control Unit Directorate General of Health Services Mohakhali, Dhaka-1212.

[37] Tozan, Y., Ratanawong, P., Sewe, M. O., Wilder-Smith, A., Kittayapong, P. (2017) Household costs of hospitalized dengue illness in semi-rural Thailand. PLoS Negl Trop Dis 11 (9): e0005961. https://doi.org/10.1371/journal.pntd.0005961.

[38] Bb.org.bd. 2020. Exchange Rate of Taka. [online] Available at: https://www.bb.org.bd/econdata/exchangerate.php [Accessed 8 September 2020].

[39] Statistics and informatice division (SID), Ministry of Planning, Government of Peoples Republic of Bangladesh, 2019, Final reports on household income and expenditure survey 2016. Dhaka: Bangladesh Bureau of Statistics (BBS), pp. 29-35.