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ORIGINAL RESEARCH ARTICLE

EPIDEMIOLOGICAL AND CLINICAL SPECTRUM OF DENGUE FEVER AT TERTIARY CARE HOSPITAL IN CHITWAN: A HOSPITAL BASED STUDY

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Received: 8 Jun, 2020	ABSTRACT
Accepted: 4 Sept, 2020	Background: Dengue fever is one of the most common tropical diseases caused by an arbo-
Published: 27 Sept, 2020	virus. This virus is a member of genus Flavivirus and <i>flaviviradae</i> family, is transmitted by bite
Key words: Dengue; Inpatients; Serological posi- tive.	of <i>Aedes degypti</i> mosquito. Its outbreak is being reported from different parts of the world including Nepal. This disease is prevalent throughout Nepal mostly in terai regions. The aim was to study the epidemiological and clinical spectrum of dengue fever at tertiary care hospital in Chitwan.
*Correspondence to: Bidhan Shrestha, Department of Medicine, Chitwan Medical College, Bharatpur-10, Chitwan, Nepal. Email: bidhansabi@gmail.com	Methods: This study was a hospital based prospective study where a total of 241 patients diagnosed with dengue fever were assessed. This study was carried out from September 2019 to February 2020. Data was entered on predesigned proforma and analyzed by using SPSS version 16.0. Mean and standard deviations was calculated for continuous variables and frequencies for categorical variables.
Citation	
	Results: More than half (56%) of the dengue patients belonged to the age group of 25-44 years.

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Out of 241 patients, 61.4% were males. Apart from fever the other common symptoms were retroorbital pain/headache comprising around 80% of patients. The mean duration of hospital stay in our study was 3.86 days. Approximately 72% (173) patients had leucopenia and 8.7% (21) had severe thrombocytopenia(<50000/cumm). NS1Ag positive were in 84% of total patients.

Conclusions: Dengue fever is one of the dreadful diseases in tropical and hilly areas of Nepal. With the help of public health authorities, educating public about vector control and immediate medical attention may help in curbing this deadly disease.

INTRODUCTION

Dengue fever is a dreadful disease caused by the Dengue virus. Dengue virus is an RNA virus, a member of *flaviviradae* family with 4 different serotypes (DENV1-4). It is transmitted to humans by a bite of a female mosquito called Aedes (Ochlerotatus) aegypti. It has an incubation period of 4-10 days.

In the late 18th century, Benjamin Rush termed dengue as "Break Bone Fever". In 2001, there was a global epidemic and by the year 2010, it was one of the 17 neglected tropical diseases.

WHO estimates more than 50 to 100 million infections worldwide every year.³ In Nepal, dengue was first identified in a Japanese traveler in 2004. The first case of dengue in Nepali population was reported in 2006 with an outbreak in 9 districts in the same year. Other massive outbreaks took place in 2006, 2010, 2013, 2016 and 2019.

The aim was to study the epidemiological and clinical spectrum of dengue fever admitted in tertiary care center of Central Nepal, hence our effort is to improve the diagnostic facilities and preventive measures and alert the citizens against this disease.

METHODS

This prospective study was carried out in Chitwan Medical College (CMC), Bharatpur, Chitwan from 1st of September 2019 to 30th of February 2020. Chitwan Medical College (CMC), being a tertiary multidisciplinary hospital, people of undiagnosed fever come from various nearby districts. The approval for the research was taken from the Ethical Review Committee of CMC. After taking informed consent, a prospective consecutive study was carried out during this six-month period. All the patients admitted in tropical ward with diagnosis of dengue fever was included during the study period.

Inclusion criteria were patients above 18 years of age, who had fever with either Dengue NS1 antigen test, IgM or IgG ELISA test positive. Exclusion criteria were age below 18 years or any coinfection with tropical diseases like Scrub typhus, Malaria, Leptospirosis, Enteric fever or other bacterial infections.

Detailed history, clinical examinations were performed in these patients. Laboratory investigations such as complete Blood count, liver function tests and ultrasound abdomen was done. Dengue NS1 test was done to those who had fever for less than 5 days, Immunoglobulin M (IgM), Immunoglobulin G (IgG) ELISA was done in patients having fever for more than 7 days and both antigen test and ELISA was done who had fever between 5 and 7 days. These patients were categorized as Dengue fever, Dengue hemorrhagic fever and Dengue Shock syndrome and managed according to the WHO protocol.

Laboratory investigations such as complete blood count and liver function tests were done at the time of admission, during hospital stay and a day before discharge to look for the improvements in leucocytes, platelet counts and transaminases level. Patients were followed up in OPD after 1 week of discharge. Data were collected by using a predesigned proforma and entered in a SPSS 16.0 (Statistical Package for Social science) version. Demographic, clinical, hematological, biochemical, and radiological parameters were assessed. Mean and standard deviation was calculated for continuous variables and frequencies for categorical variables.

RESULTS

In our study, a total of 241 patients admitted were diagnosed with dengue fever during the six months period. The age and sex distribution of the patients is depicted in Table 1. The mean age of the patients was calculated as 34.44 years on the basis of descriptive statistics. More than half (56%) of the dengue patients belonged to the age group of 25-44 years. Dengue was more commonly seen in male than in females (61.4% Vs 38.6%) with male: female ratio of 1.6:1.

Table 1: Age and sex distribution of dengue cases (n=241)

Age Group (in years)			
	Male (%)	Female (%)	Total (%)
15-24	34	22	56(23.23)
25-34	52	32	84(34.85)
35-44	31	21	52(21.57)
45-54	18	10	28(11.61)
55-64	7	5	12(4.97)
>/=65	6	3	09(3.73)
Total	148(61.4)	93(38.6)	241(100)



Figure 1: Distribution of dengue cases according to symptoms

As the clinical features are concerned, all the patients had come with fever with one or more associated symptoms as shown in

Figure 1 below. The mean duration of the fever was 3.58 days. Another common complaint in our study was retro-orbital pain present in 203 patients (84.2%) followed by headache (80.1%), myalgia (61%) and vomiting (39%).

Table 2 showed most patients being admitted were from Chitwan district (68.46%), followed by Makwanpur (13.27%) and Nawalparasi district (10.37%).

Table 2: District wise distribution of dengue cases

Districts	Frequency (%)
Chitwan	165(68.46)
Makwanpur	32(13.27)
Nawalparasi	25(10.37)
Gorkha	05(2.07)
Butwal	03(1.24)
Bara	05(2.07)
Tanahun	04(1.65)
Dang	01(0.41)
Dhading	01(0.41)
Total	241(100)

Table 3 showed the laboratory parameters of the patients. The most common hematological abnormality was leucopenia (71.8%).

Table 3: Abnormal laboratory parameters of dengue cases

Laboratory Parameters	Frequency (%)	
Leucopenia (<4000 cmm)		173(71.8)
Leucocytosis (>11000 cmm)		3(1.2)
Thrombocytopenia (mm³)	1,00,000-1,50,000	129(53.5)
	50,000-1,00,000	91(37.8)
	<50,000	21(8.7)
AST(>37 IU/L)		116(48.1)
ALT(>42 IU/L)		110(45.6)

Table 4: Patient distribution according to days of fever

Days of Fever	Number of patients (%)		
1	3(1.2)		
2	36(14.9)		
3	88(36.5)		
4	21(8.7)		
5	52(21.6)		
6	39(16.2)		
7	2(0.8)		
Total	241(100)		

The Table 4 showed the days when patients presented to the hospital with fever. More than 60% of patient presented be-

fore fifth day of onset of fever so as per protocol these patients were tested for NS1 antigen only. From 5 to 7th day around 39 % of patients presented with fever. None presented after 7th day. This corrugates well with the positivity of serological test done depending on the days of duration of fever. Serological profile of the patient is depicted below in Figure 2.



Figure 2: Serological Profile of Dengue Fever Patients

The most common type of serology which was positive was NS1 Antigen test (84%). 23 patients (9.5%) were positive for both NS1 and IgM antibody.

USG findings	No of patients (%)	
Ascites	1 (0.4)	
GB Edema	37 (15.4)	
Hepatomegaly	35 (14.5)	
Normal	168 (69.7)	
Total	241 (100.0)	

Table 5: USG Findings in Dengue

The Ultrasonographic (USG) findings, out of the total 241 patients, most of them(69.7%) had normal USG findings. Gall bladder edema was seen in 37 (15.4%) patients, 35(14.5%) had hepatomegaly and only one patient had ascites. The details of USG findings according to the positive serological tests is shown below in Table 6.

Table 6: USG Findings on the basis of positive serology

USG	NS1	lgM	lgG	lgG+lgM	NS1+IgM
Ascites	1	0	1	0	0
GB Edema	14	7	37	2	13
Hepatomegaly	26	2	35	0	5

Out of 241 patients, most of them recovered and were discharged. Only one patient died.

DISCUSSION

During the study period of six months, 241 febrile patients diagnosed with dengue fever were admitted in the ward. Age of the patients ranged from 18 to 72 years. The most affected age group was 25-44 years (56%). These findings are similar to the study conducted by Mehta et al. and Deshwal et al. This age group being, a productive phase with a high male preponderance, work outside their houses and are more susceptible to mosquito bites. However, a study done in Kolkata had majority of cases between 11 to 30 years.

Out of total admitted 148 patients (62%) were male and 93 (38%) were female with the ratio of 1.6:1 respectively. Similar results were observed in studies by Chitkara et al , Chrispal et al. and Ittyachen et al. A study done by Chaterjee et al. showed equal sex distribution whereas a South American study showed more infection in females than males.

Around 68% of patients with dengue fever were from Chitwan followed by neighboring districts such as Makwanpur, Nawalparasi, Gorkha, Butwal, Bara and Tanahu respectively which imply that this virus is not limited to terai regions only. This may be due to travel to an endemic area, urbanization and prevalence of marshy areas where mosquitoes breed and multiply easily.⁵

The mean duration of hospital stay in our study was 3.86 days conflicting with the study done by Mehta et al.¹⁰ This could be because of non-availability of beds in our hospital during the outbreak of dengue fever and early improvement of patients leading to early discharge of the patients.

The mean duration of fever was 3.58 days. However a research conducted in Sri Lanka by Kularatne et al.3 and in North India by Awasthi et al. showed a mean duration of fever of 7 and 10 days respectively. In this study all the patients had fever with less than 20% accounting for itching, cough and diarrhea. These findings are comparable to the study done by Nepal et al. In contrast the studies by Jayadas et al and Pande et al found vomiting and a study in Kerala showed gastrointestinal symptoms as the most common symptoms.

Leucopenia in 173 patients(72%) was the most common laboratory finding consistent with studies performed by Karoli et al. and Singh N et al. A study by Dhivya et al. showed leucopenia in only 36% of study population, lesser than as compared to our study. Leucopenia was most commonly observed because of the direct suppression of bone marrow by the virus.²⁰

Thrombocytopenia was most commonly seen in studies conducted by Jayadas, et al.²⁰, Kumar et al . and Laul et al. However in this present study thrombocytopenia was the second most common manifestations. Bone marrow suppression, immune mediated clearance and spontaneous aggregation of platelets to virus infected endothelium may be responsible for such thrombocytopenia.

The severity of dengue fever is predicted by severe thrombo-

cytopenia. In a study done by Mandal et al there was severe thrombocytopenia in 38% of patients. We have found only 21 patients (8.7%) having severe thrombocytopenia (<50000/ cu.mm) suggestive of lesser severity and low mortality rate in our study.

Liver enzymes such as Aspartate Transaminase (AST) and Alanine Transaminase (ALT) was elevated in more than 45% of cases in our study. Similar results was seen in the studies by Laul et al.²⁷ Jayadas et al.²⁰ found elevated AST than ALT level in accordance to our study and this may be secondary to release of AST from the parts other than liver (heart and striated muscles). Deranged liver function in dengue infection can be a result of the direct attack of the virus on liver cells or the unregulated host immune response against the virus. Fulminant hepatic failure occurs because of acute severe hepatitis and massive necrosis of the liver, causing hepatic encephalopathy and even death.²²

The most common peak season for dengue infection in this study was in the month of mid-August to last week of September. This kind of seasonal response was seen in research conducted by Gupta et al. and studies from tropical countries like India, China and Philippines ., These months are the post monsoon period in Nepal where mosquitoes have a favourable climate to breed and multiply thus serving as a vector for transmission of virus in humans.⁵

The most common type of serological test to be positive in this study was Dengue NS1 antigen test. NS1antigen test was positive in 201 patients-(84%) followed by combined NS1 and IgM positivity in 23 patients (9.5%). Similar result was shown in North Indian study and a study conducted by Chhotala et al.⁴ The higher NS1 positivity may be because many patients came to our hospital and got admitted within two or three days of fever when this particular test is specifically done aiding for early identification and prompt notification. There are also evidences that sensitivity of NS1 antigen test is higher in primary infection(>90%) and even correlated with higher levels of viral load.

Dengue IgM antibody test was positive in only 11 patients (4.5%) in our study. A study published in 2012 by Shah et al. 6 showed seropositivity of Dengue IgM cases to be 9% which was twice than our study.

The ultrasound findings in our study simulated with the study done by Laul et.al.²⁷ Hepatomegaly and GB edema may be due to direct viral invasion of gall bladder and liver leading to protein rich plasma leak causing increase in severity.²⁴

Out of 241 dengue cases admitted for a certain period in the ward there was only 1 death with a case fatality rate of 0.41% similar to the research conducted by Antony et al. and studies conducted in Jakarta and West Bengal. Our patient was 71 years old male, a known hypertensive, with history of fever for seven days and shortness of breath. He had thrombocytopenia, deranged liver and renal function tests with positive NS1 test and was admitted in medical intensive care unit (MICU) with the diagnosis of Dengue shock syndrome. He was monitored with central line, transfused with four pints of PRP, IV antibiotics, double ionotrope support and kept in Mechanical Ventilation. But despite all the treatment, patients died after 2 days in MICU. No mortality was recorded in a study conducted by Ratageri et al. and Khan et al. The overall mortality of dengue infection is low if treated appropriately and early, however the mortality due to DHF and DSS may be high.

It was a single centered study. Non availability of Dengue viral RNA study by RT-PCR (Reverse Transcriptase-Polymerase chain reaction) was the major limitation in our study. With this test we could have distinguished the various serotypes and the severity of different strains of virus.

CONCLUSION

Dengue, an arthropod borne viral disease poses a significant morbidity and a high financial burden. With each outbreak, the number of confirmed cases have increased significantly. In our analysis, Leucopenia, rather than thrombocytopenia was the most common laboratory finding. Furthermore, the study also showed cases from the hilly areas implying that dengue was not limited to terai regions only. Hence, there should be a proper surveillance of the infection, start an integrated vector control programme, make an awareness programme and emergency preparedness for this cyclical outbreak.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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