CLINICO-LABORATORY OBSERVATIONS AND OUTCOME OF DENGUE INFECTION IN A TERTIARY CARE HOSPITAL OF WESTERN NEPAL: AN OBSERVATIONAL CROSS-SECTIONAL STUDY

Niraj Kumar Jaiswal[1], Shatdal Chaudhary[2], Nagendra Chaudhary[3]

ABSTRACT:

INTRODUCTION:

Dengue fever (DF) is highly prevalent in tropical and subtropical countries all over the world. This study was done to study the clinico-laboratory profile of DF patients and their outcomes in a tertiary care hospital of western Nepal.

MATERIAL & METHODS:

A prospective observational cross-sectional study conducted over 6 months (October 2016 to March 2017) in patients admitted to medical inpatient ward of a tertiary care referral hospital located at south west Nepal. All febrile patients underwent dengue antibody (IgM) testing. Patient details, clinical manifestations and laboratory parameters were recorded. Descriptive analysis was done as mean and percentage.

RESULTS:

Out of total 2653 hospital admissions, 1274 patients (male: 780, female: 494) presented with fever. Forty patients between 17 years to 84 years (Mean age ± SD: 40.3±17 years) were diagnosed as DF. All the age groups were almost equally affected. The average duration of hospital stay was 5.4±3.2 days**.** Fever (n=40, 100%), body ache (n=29, 74.4%) and headache (n=28, 70%) were three leading complaints in dengue patients. Only 22.5% (n=9) of the patients had thrombocytopenia (mild and moderate). Severe thrombocytopenia was not noticed. Only 10% of total dengue cases received platelet transfusion. The mean platelet count increased from day one to day seven gradually. All the patients recovered.

CONCLUSION:

DF is a well-established vector-borne disease in south west Nepal; may be due to rapid urbanization and poor hygiene facility. Appropriate disease control programme emphasizing on vector surveillance and control, early clinical diagnosis and treatment reduces the dengue-related deaths.

KEY WORDS: Dengue fever, thrombocytopenia, bleeding manifestations

1. Lecturer, Department of Internal Medicine, Universal College of Medical Sciences, Bhairahawa, Nepal
2. Associate Professor, Department of Internal Medicine, Universal College of Medical Sciences, Bhairahawa, Nepal
3. Lecturer, Department of Pediatrics, Universal College of Medical Sciences, Bhairahawa, Nepal

For Correspondence
Dr. Nagendra Chaudhary
Lecturer
Department of Paediatrics
Universal College of Medical Sciences
Bhairahawa 32900, Nepal
E-mail: enagendra@hotmail.com

INTRODUCTION

Dengue fever (DF), a vector-borne disease transmitted by Aedes aegypti species of infected mosquitos, is highly prevalent in tropical and sub-tropical countries all over the world causing major public health concern [1]. Brady OJ et al (2012) reported the annual dengue infection to be around one hundred millions globally[2]. The public health concern for increase in dengue cases has recently increased due to migration and urbanization [3].

The vector, *Aedes aegypti* mosquito, is a day time feeder which lives in urban areas and breeds mostly in man-made containers [4]. Temperature and rainfall are the most significant factors for vectors development and transmission [5,6]. Increase in population density and low socioeconomic status also play an important role in rise in dengue cases [7,8]. DF can present with wide variations in clinical manifestations ranging from viral prodromal manifestations to haemorrhage and shock. DF in Nepal was first reported in 2004 which has been rapidly increasing in various geographical regions over years [9].

All the four serotypes of dengue virus circulate in Nepal with increased disease burden [10, 11]. Dengue virus serotype 1 was generally seen in the 2010 outbreak and later on serotype 2 was detected in the 2013 outbreaks suggesting serotype shifts. This serotype shift is generally responsible for the severity of the disease [12]. It is, now, a firmly established disease of tropical and subtropical regions of Nepal and is also reported in many hilly regions (eg. Kathmandu) due to climate change and migration [13, 14]. This study was undertaken to study the clinico-laboratory profile of DF patients and their outcomes in a tertiary care hospital of western Nepal.

MATERIAL & METHODS:

A prospective observational cross-sectional study was conducted over 6 months (October 2016 to march 2017) in patients admitted to medical inpatient ward of Universal College of Medical Sciences, a tertiary care referral hospital located at south west Nepal. All febrile patients underwent dengue antibody (IgM) testing. A case was included, if patients presented with fever and positive dengue serological test (IgM Elisa). Patients with fever but negative dengue serological test were excluded from analysis. Written and informed consent was obtained from all patients included in the study. The study was approved by the Institutional review board. Complete blood count and platelet counts were done at admission, day 3 and day 7. Patient details, clinical manifestations and laboratory parameters were entered in Excel sheet. Stata V13 was used for analysis. Descriptive analysis was done as mean and percentage.

RESULTS:

Out of total 2653 hospital admissions (male: 1356, female: 1297) in medical ward, 1274 patients (male: 780, female: 494) presented with fever. 40 patients between 17 years to 84 years (Mean age ± SD: 40.3±17 years) were diagnosed as dengue fever and were included for final analysis. All the age groups were almost equally affected; 35% in 17-32 years and 32.5% in both 33-47 years and 48-84 years with female preponderance (male: female: 0.5:1). The average duration of hospital stay in patients with dengue was 5.4±3.2 days **(Table 1).**

Description	Total No (%)
Age groups	
17-32 years	14 (35.0)
33-47 years	13 (32.5)
48-84 years	13 (32.5)
Mean age ±SD (years)	40.3±17.0
Gender	
Male	14 (35.0)
Female	26 (65.0)
Religion	
Hindu	36 (90.0)
Muslim	4 (10.0)
Marital status	
Married	33 (82.5)
Unmarried	7 (17.5)
Duration of stay in hospital (mean ±SD in days)	5.4±3.2

Table 1. Baseline characteristics of dengue patients

Fever (n=40, 100%), body ache (n=29, 74.4%) and headache (n=28, 70%) were three leading complaints in dengue patients. Body rashes (n=3, 7.5%), joint pain (n=2, 5%), abdominal pain (n=4, 10%), and retro-orbital pain (n=1, 2%) along with spontaneous bleeding (n=2, 5%) were minor

clinical manifestations (**Table 2).**

Symptoms	No (%)	Duration in days (Mean±SD)
Fever	40(100)	4.4±3.2
Headache	28 (70.0)	3.7±2.8
Altered sensorium	7 (17.5)	4.2 ± 2.8
Body ache	29 (74.4)	3.1 ± 2.5
Rash	3 (7.5)	2.3 ± 0.6
Spontaneous bleeding	2 (5.0)	
Joint pain	2 (5)	
Abdominal pain	4(10)	
Seizure	1(2)	
Retro-orbital pain	1(2)	

Table 2. Clinical profile of dengue patients

Only 22.5% (n=9) of the patients had thrombocytopenia (mild and moderate). Severe thrombocytopenia was not noticed. Only 10% of total dengue cases received platelet transfusion. The mean platelet count increased from day one to day seven gradually **(Table 3).** All the patients recovered and were discharged suggesting 100% cure.

	Mean ± SD
Pulse rate	84.6 ± 11.7
Systolic blood pressure	115 ± 16.9
Diastolic blood pressure	72.4 ± 11.5
Temperature	99.5 ± 1.4
Respiratory rate	19.5 ± 3.3
Hemoglobin	11.9 ± 1.8
HCT	36.4 ± 5.1
Total Leucocytic count	8977.5 ± 4499.5
Neutrophils (%)	67.0 ± 15.3
Lymphocytes (%)	30.3 ± 14.8
Monocytes (%)	0.75 ± 0.9
Platelet counts (Day 1)	176775 ± 72674.4
Platelet counts (Day 3)	196200 ± 90533.8
Platelet counts (Day 7)	254400 ± 81326.4
Thrombocytopenia, n (%)	9 (22.5%)
Mild	5 (55.6%)
Moderate	4 (44.4%)

Table 3. Clinical and biochemical characteristics of dengue patients

DISCUSSION:

Dengue fever (DF) is an infectious disease with increased occurrence in tropical and subtropical regions of developing countries like Nepal. The increase frequency of complications and development of severe dengue in developing nations could be due to the lack of appropriate technical support and scientific basis for the proper management of cases with hemorrhagic manifestations.

DF is an emerging disease in Nepal and various reports on its increasing incidence have been reported from previous studies conducted in the nation. A recent study conducted in Nepal suggested a high prevalence in the range of 26.1-55.4% in all febrile patients suspected to have DF [15]. The prevalence of DF in the present study was 1.5% in all inpatient admission to medical ward and was double (3.139%) in all admitted febrile patients.

In the present study, 65% (n=26) females presented with DF which was higher than the previous studies conducted by Fugimoto and Koifman [16] and Chairulfatah A et al [17]. The occurrence of DF in females was 3-fold higher (5.26% vs1.79%) in comparison to males in the present study whereas a study conducted on dengue outbreak in India [18] suggested male preponderance. Studies conducted by Kashinkunti et al [19] and Gurdeep et al [20] also suggested more number of males affected with DF. This suggests the sexual variation in the occurrence of DF in different geographical regionS [19, 20]. The reason of higher occurrence of DF in Nepalese females could be due to involvement in household and outdoor activities in fields which predisposes them to higher chance of being bitten with infected mosquitoes.

In the present study, DF cases uniformly occurred from 17-84 years. Age group sub classification showed 35% of cases in age groups 17-32 years and 32.5% in both age groups 33-47 years and 48-84 years. A study conducted by Neupane et al (2013) showed majority of DF cases to be detected in the age groups 15-50 years [21]. Khan et al (2008) reported the occurrence of DF in younger population (median age 24 years; range: 6-94 years) during an outbreak in Saudia Arabia [22]. Uddin et al [23] also reported that 72% of younger population (Less than 40 years) were positive for dengue. In our study, we could not include younger children less than 17 years. Another study done by Mallhi et al [24] showed older age (>40 years; OR: 4.1, P<0.001) as an independent predictor of dengue occurrence. This suggests that DF can affect both children as well as adults and elderly whenever exposed to infected

mosquitoes.

The mean duration of hospital admissions for DF patients in the present study was 5.4±3.2 days which was nearly similar to a recent study conducted by Aroor et al [25]. Tripathi et al (1998) [18] had reported shorter hospital admission duration (3.4 days) which could be due to earlier death of eleven patients just within 9.8 hours of presentation. The hospital stay of dengue has now increased when compared to the past due to improvement in the management of such cases and decreased dengue related deaths.

Fever, myalgia and headache are the predominant clinical manifestations in DF patients (23,2628). In the present study too, fever was the predominant clinical manifestation followed by body ache and headache. In a study done by Deshwal et al [26], fever headache and myalgia were top three clinical presentations in dengue patients which were almost similar to the present study.

Rashes are also important findings in DF patients. The proportion of patients with rashes (n=3, 7.5%) in our study was less than the study done by Deshwal et al [26]. Rashes (45%) occurrence in a study by Uddin et al [23] was even more than the present study and study done by Deshwal et al. This could be explained by probably less sample size in our study compared to their study.

Although thrombocytopenia is an important finding in DF, we noticed it only in 22.5% cases whereas Deshwal et al [26] in their study found that 69.5% cases had the same. The patients with dengue having thrombocytopenia was almost similar in the present study and the study done by Kuna et al (Poland) [27]. A recent retrospective study conducted by Unnikrishnan et al [28] found thrombocytopenia in 90% of cases which was even higher than the present study and study done by Deshwal et al [26]. Thrombocytopenia in all cases (100%) also has been reported in literature [23]. The reason for occurrence of thrombocytopenia only in minority of cases in the present study could be due to their earlier presentation to hospital and none of them presenting with shock. Infection by a single serotype rather than mixed infection could also be the reason for the benign presentation of the disease. Thrombocytopenia in DF is believed to be caused due to IgM anti-platelet antibodies which induce platelet lysis via complement activation [29].

Insignificant bleeding manifestation in the present study could also be explained due to the lower percentage of thrombocytopenia and none with severe thrombocytopenia. Thrombocytopenia was well correlated with bleeding manifestations in a study conducted by Duthade et al [30].

Dengue outbreak generally occurs in the post monsoon [6]. In the present study, we found increased number of dengue during the months of November and December. It could be due to breeding of dengue mosquitoes in containers nearby home and in other water stagnant area.

Management of DF is supportive. In the present study, all cases received supportive treatment. Only 10% of cases required platelet transfusion. None of them had dengue shock syndrome. No mortality was observed. High mortality generally seen in severe dengue (dengue hemorrhagic fever, dengue shock syndrome) could be due to disseminated intravascular coagulation, intracranial hemorrhage, and massive gastrointestinal hemorrhage [18,31].

CONCLUSION:

Over the past few years, there is a trend of increased number of DF cases in south west Nepal due to rapid urbanization and poor hygiene facility. Fever, headache and body ache followed by rashes, joint pains and bleeding manifestations along with thrombocytopenia from this region alarm for the possibility of dengue fever. Management is totally supportive. Although thrombocytopenia is common, only minority require platelet transfusion. Appropriate disease control programme emphasizing on vector surveillance and control, early clinical diagnosis and treatment reduces the dengue-related deaths.

ACKNOWLEDGEMENTS:

The authors thank Mr. Shankar Prasad Joshi, record section of UCMS, for providing necessary data during the study. We also thank Dr. Karan Pokharel for helping in data collection.

CONFLICTS OF INTEREST:

The authors declare that there is no conflict of interest regarding the publication of this article.

REFERENCES:

1. *Gubler DJ. Dengue and dengue hemorrhagic fever. Clin Microbiol Rev. 1998 Jul;11(3):480-96.*

2. *Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis. 2012;6(8):e1760.*

3. *Naish S, Dale P, Mackenzie JS, McBride J, Mengersen K, Tong S. Climate change and dengue: a critical and systematic review of quantitative modelling approaches. BMC Infect Dis. 2014 Mar 26;14:16-7.*

4. *Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ, et al. Dengue: a continuing global threat. Nat Rev Microbiol. 2010 Dec;8(12 Suppl):S7-16.*

5. *Bai L, Morton LC, Liu Q. Climate change and mosquito-borne diseases in China: a review. Glob Health. 2013 Mar 9;9:10.*

6. *Morin CW, Comrie AC, Ernst K. Climate and dengue transmission: evidence and implications. Environ Health Perspect. 2013 Dec 12:1(1112):1264-72.*

7. *Méndez-Lázaro P, Muller-Karger FE, Otis D, McCarthy MJ, Peña-Orellana M. Assessing climate variability effects on dengue incidence in San Juan, Puerto Rico. Int J Environ Res Public Health. 2014 Sep 11;11(9):9409-28.*

8. *de Melo DPO, Scherrer LR, Eiras ÁE. Dengue fever occurrence and vector detection by larval survey, ovitrap and MosquiTRAP: a space-time clusters analysis. PloS One. 2012;7(7):e42125.*

9. *Pandey BD, Rai SK, Morita K, Kurane I. First case of Dengue virus infection in Nepal. Nepal Med Coll J NMCJ. 2004 Dec;6(2):157-9.*

10. *Malla S, Thakur GD, Shrestha SK, Banjeree MK, Thapa LB, Gongal G, et al. Identification of All Dengue Serotypes in Nepal. Emerg Infect Dis. 2008 Oct;14(10):1669-70.*

11. *Pun SB. Dengue: an emerging disease in Nepal. JNMA J Nepal Med Assoc. 2011 Dec;51(184):203-8.*

12. *Gupta BP, Singh S, Kurmi R, Malla R, Sreekumar E, Manandhar KD. Re-emergence of dengue virus serotype 2 strains in the 2013 outbreak in Nepal. Indian J Med Res. 2015 Dec;142 Suppl:S1-6.*

13. *Dhimal M, Ahrens B, Kuch U. Climate Change and Spatiotemporal Distributions of Vector-Borne Diseases in Nepal--A Systematic Synthesis of Literature. PloS One. 2015;10(6):e0129869.*

14. *Dumre SP, Shakya G, Na-Bangchang K, Eursitthichai V, Rudi Grams H, Upreti SR, et al. Dengue virus and Japanese encephalitis virus epidemiological shifts in Nepal: a case of opposing trends. Am J Trop Med Hyg. 2013 Apr;88(4):677-80.*

15. *Pandey BD, Pandey K, Neupane B, Shah Y, Adhikary KP, Gautam I, et al. Persistent dengue emergence: the 7 years surrounding the 2010 epidemic in Nepal. Trans R Soc Trop Med Hyg. 2015 Dec;109(12):775-82.*

16. *Fujimoto DE, Koifman S. Clinical and laboratory characteristics of patients with dengue hemorrhagic fever manifestations and their transfusion profile. Rev Bras Hematol E Hemoter. 2014 Mar;36(2):115-20.*

17. *Chairulfatah A, Setiabudi D, Agoes R, Colebunders R. Thrombocytopenia and Platelet Transfusions in Dengue Haemorrhagic Fever and Dengue Shock Syndrome. Dengue Bulletin. 2003;27:138-43.*

18. *Tripathi BK, Gupta B, Sinha RS, Prasad S, Sharma DK. Experience in adult population in dengue outbreak in Delhi. J Assoc Physicians India. 1998 Mar;46(3):273-6.*

19. *Kashinkunti MD, Shiddappa, Dhananjaya M. A study of clinical profile of dengue fever in a tertiary care teaching hospital. Sch J App Med Sci 2013; 1(4):280-2.*

20. *Gurdeep S, Dhooria, Deepak Bhat, Harmesh S Bains. Clinical profile and outcome in children of dengue hemorrhagic fever in north India. Iran J Pediatr. 2008;18:222-8.*

21. *Neupane B, Rijal KR, Aryal GB, Shah Y, Banjara MR, Sherchand JB, Moritad K, Pandeyb BD. Clinical and laboratory features of dengue fever in the southern lowlands of Nepal. Dengue. 2013;37:1.*

22. *Khan NA, Azhar EI, El-Fiky S, Madani HH, Abuljadial MA, Ashshi AM, et al. Clinical profile and outcome of hospitalized patients during first outbreak of dengue in Makkah, Saudi Arabia. Acta Trop. 2008 Jan;105(1):39-44.*

23. *Uddin MN, Hossain MM, Dastider R, Hasan Z, Ahmed Z, Dhar DK. Clinico-pathological profile of dengue syndrome: an experience in a tertiary care hospital, Dhaka, Bangladesh. Mymensingh Med J MMJ. 2014 Oct;23(4):774-80.*

24. *Mallhi TH, Khan AH, Adnan AS, Sarriff A, Khan YH, Jummaat F. Clinico-laboratory spectrum of dengue viral infection and risk factors associated with dengue hemorrhagic fever: a retrospective study. BMC Infect Dis. 2015 Sep 30;15:399.*

25. *Aroor AR, Saya RP, Sharma A, Venkatesh A, Alva R. Clinical Manifestations and Predictors of Thrombocytopenia in Hospitalized Adults with Dengue Fever. North Am J Med Sci. 2015 Dec;7(12):547-52.*

26. *Deshwal R, Qureshi MI, Singh R. Clinical and Laboratory Profile of Dengue Fever. J Assoc Physicians India. 2015 Dec;63(12):30-2.*

27. *Kuna A, Bykowska M, Kulawiak N, Biernat B, Szostakowska B, Nahorski WL, et al. Clinico-laboratory profile of dengue patients returning from tropical areas to Poland during 2010-15. J Vector Borne Dis. 2016 Sep;53(3):234-9.*

28. *Unnikrishnan R, Faizal BP, Vijayakumar P, Paul G, Sharma RN. Clinical and laboratory profile of dengue in the elderly. J Fam Med Prim Care. 2015;4(3):369-72.*

29. *Lei HY, Huang KJ, Lin YS, Yeh TM, Liu HS, Liu CC. Immunopathogenesis of dengue hemorrhagic fever. Am J Infect Dis. 2008;4(1):1-9.*

30. *Duthade MM, Bhakare JK, Damle AS. Clinical profile of dengue haemorrhagic fever from Jan 2009 to Dec 2009 in and around Aurangabad. J Commun Dis. 2011 Jun;43(2):131-4.*

31. *Navarrete-Espinosa J, Gómez-Dantés H, Celis-Quintal JG, Vázquez-Martínez JL. Clinical profile of dengue hemorrhagic fever cases in Mexico. Salud Publica Mex. 2005 Jun;47(3):193-200.*