



Clinico-epidemiological study of Dengue outbreaks- an overview from Kumaon region of Uttarakhand

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Abstract

Objectives: a) To know about the certain demographic details of dengue cases
b) To determine the clinical profile of the cases.
c) To assess the hospital stay period and the outcome of these cases

Material & Methods

Study Design: Cross-sectional observational (record based)

Blood samples were collected from the clinically suspected dengue cases were tested for NS1 antigen and IgM MAC ELISA. Necessary investigations like USG, blood were also carried out. Standard WHO definition were used to define dengue, DHF and DSS.

Observations: A total of 239 patients, attending STGH Hospital, Haldwani between August and December 2015 and 97 patients in the 2 months in 2010 were included in the study. Dengue was suspected when two or more of the following symptoms were present: fever, retro-orbital pain, myalgia, arthralgia, skin rash, nausea/vomiting, and hemorrhagic manifestations. Complete blood counts and liver function tests were carried out. In the year 2015 the percentage of DHF-I and DHF-II cases in the study was 7.53% (n=18) and 1.67% (n=4) respectively with a total of 9.2% while the DSS cases were 3.25%(n=8). Whereas the proportion of DHF cases in 2010 was 12.36% higher than in 2015 but no severe DSS was found. As the severity and number of dengue cases with DSS was less in the year 2010 the period of stay in the hospital was comparatively lesser than in 2015.

Conclusions: In the study the pattern of dengue cases in the two outbreaks in different years was seen more in the active age group and males having more outdoor activity were more affected with dengue infection. Certain concomitant conditions like hepatitis, scrub typhus, malaria infection was also observed in dengue cases. Public awareness and public education regarding dengue is of utmost importance for prevention as well as for management of dengue fever.

Keywords: Dengue fever, Thrombocytopenia, Dengue shock syndrome (DSS), Dengue hemorrhagic fever (DHF).

Introduction

Dengue fever (DF), also known as breakbone fever, is an infectious tropical disease, caused by the dengue virus. Symptoms include fever, headache, muscle and joint pains, and a characteristic skin rash (similar to measles). In smaller proportion of cases, the disease develops into the life threatening dengue hemorrhagic fever (DHF) resulting in bleeding low levels of blood platelets and blood plasma leakage, or into dengue shock syndrome (DSS), where dangerously low blood pressure occurs.¹ It is a globally important arbovirus infection transmitted by mosquitoes of the Aedes genus (primarily Aedes aegyptii but also Aedes albopictus), an insect found in tropical and subtropical regions. Around one-half of the world's population those in tropical and subtropical countries is at risk of dengue infection.² One recent estimate indicates 390 million dengue infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease). Another study, of the prevalence of dengue, estimates that 3.9 billion people, in 128 countries are at risk of infection with dengue viruses.²

It is a major public health problem in South East Asia, especially in India where there is a reported case fatality ratio of 3-5%.² Dengue infection is endemic in many parts of India. In India, the first epidemic of clinical dengue like illness was recorded in Madras (now Chennai) in 1780. The first virologically proven epidemic of dengue fever in India occurred in 1963-64, outbreaks have been reported from different parts of the country at regular intervals.^{3 to 9}

Dengue outbreaks may be explosive or progressive depending on the density and efficiency by the vector can be infected, the serotype and strain of the dengue virus, the number of susceptibles (non immune) humans in the populations and the amount of vector human contact¹⁰. A change in the predominant circulating serotype, unprecedented rains, enormous infrastructure development and increased reporting due to

improved diagnostic facilities were the factors responsible for the increased and unexpected dengue outbreaks in the country.

Towards the concern of emerging diseases, WHO has framed the theme “Emerging Diseases: Global response” in 2005. New emerging diseases like Ebola virus disease not transmitted by mosquito vector, Zika virus disease due to Aedes mosquito are surfacing up in the list of existing emerging diseases in which dengue is the commonest health problem as due to the highly anthrophilic activity of Aedes mosquito dengue outbreaks are quite often. So, in Uttarakhand being mountainous terrain state not favouring the growth of mosquitos (cold blooded vector) dengue cases have occurred laggely in the year 2010 and 2015. So, the focus has been made in this direction regarding the pattern of dengue outbreak in Kumaon region in Uttarakhand state.

Objectives

- To know about the certain demographic details of dengue cases
- To determine the clinical profile of the cases.
- To assess the hospital stay period and the outcome of these cases

Material and Methods

Study Design: Cross-sectional observational (record based)

Study Duration: 2 months in 2010 and 5 months in 2015

Study Area:- STMGH (Dr. Susheela Tiwari Memorial Government Hospital) Haldwani

Study setting:- Medicine wards of STMG Hospital, Haldwani

Study subjects:- Either the case positive on rapid test NS1 or serologically confirmed dengue cases in >15 years of age of both sexes

Study variables: demographic and clinical and necessary investigation details, serological information,

Methodology: Blood samples were collected from the clinically suspected dengue cases were

tested for NS1 antigen and IgM MAC ELISA. Necessary investigations like USG, blood were also carried out. Standard WHO definition were used to define dengue, DHF and DSS.

A total of 239 patients, attending STH Hospital, Haldwani between August and December 2015 and 97 patients in the 2 months in 2010 were included in the study. Dengue was suspected when two or more of the following symptoms were present: fever, retro-orbital pain, myalgia, arthralgia, skin rash, nausea/vomiting, and hemorrhagic manifestations. Complete blood counts and liver function tests were carried out.

In the year 2010 information of the dengue cases was taken in the prescribed format of IDSP whereas in the year 2015 the data was collected from the admitted cases in dical wards under medicine department.

WHO standard definitions has been used for defining the DHF-1 and DHF-II and DSS.¹¹

Probable dengue: An acute febrile illness with 2 or more of the following manifestations like headache, retro-orbital pain, myalgia, arthralgia, rash, haemorrhagic manifestations and leucopenia.

Confirmed dengue:- A probable case confirmed by one of the following laboratory criteria :-

- Demonstration of dengue virus antigen from serum samples by rapid NS1 tests/ELISA method
- At least 4 fold change in reciprocal IgG/IgM titres in paired samples

DHF:- A case meeting all the 4 of the following criteria :-

- Fever or history of fever lasting 2-7 days occasionally biphasic
- Haemorrhagic tendency by one of the following like positive tourniquet test, petachie, ecchymosis or purpura, bleeding from the mucosa, gastrointestinal tract or other locations or hemetemesis or malaena.
- Thrombocytopenia ≤ 10000 cells/cu mm
- Evidence of plasma leakage owing to increased vascular permeability shown by increased hematocrit $\geq 20\%$ above average for age/sex, a decrease in the hematocrit

after intervention $\geq 20\%$ of baseline, signs of plasma leakage such as pleural effusion, ascites or hypoproteinemia.

DSS: All the 4 criteria for DHF must be met, in addition to evidence of circulatory failure manifested.

By rapid/weak pulse, narrow pulse pressure, hypotension for age, cold clammy skin and restlessness.

Statistical Analysis: The data so collected was checked for missing information and was used for obtaining the required epidemiological information of the taken dengue cases so that the data can be presented in the form of percentages. The software used is MS excel and SPSS v-18 (IBM trial version)

Ethical Clearance: Necessary ethical approval has been obtained.

Results

Table -1 Age and sex wise and district wise distribution of dengue cases in both the years

Age-groups (in years)	2010	2015
	Number (%) n =97	Number (%) n =239
10-20	22 (22.68%)	37 (15.48%)
21-30	37 (38.14%)	99 (41.42%)
31-40	19 (19.59%)	50 (20.92%)
41-50	10 (10.31%)	35 (14.65%)
51-60	7 (7.22%)	13 (5.44%)
61-70	2 (2.06%)	4 (1.67%)
>70yrs	0 (0%)	1 (0.42%)
Total	97 (100%)	239 (100%)
Sex wise	2010	2015
	Number (%)	Number (%)
Males	75 (77.3%)	168 (70.3%)
Female	22 (22.7%)	71 (29.7)
Total	97 (100%)	239 (100%)
District wise dengue cases	2010	2015
	Number (%)	Number (%)
Almora	2 (2.06%)	9 (3.76%)
Bageshwar	0 (0%)	2 (0.84%)
Adjoining states (UP/Nepal)	8 (8.25%)	15 (6.28%)
US nagar	8 (8.25%)	58 (24.27%)
Chamoli	0 (0%)	1 (0.42%)
Champawat	5 (5.15%)	2 (0.84%)
Nainital	74 (76.29%)	148 (61.92%)
Pithoragarh	0 (0%)	4 (1.67%)
Total	97 (100.0%)	239 (100.0%)

The frequency of dengue cases was reported more in the age range of 10 to 50 years as compared to >50 years age in both the years (2010 and 2015). Maximum cases occurred in the age group 21-30 years that is 38.14% (n=37) and 41.42% (n=99) in the 2010 and 2015 respectively.

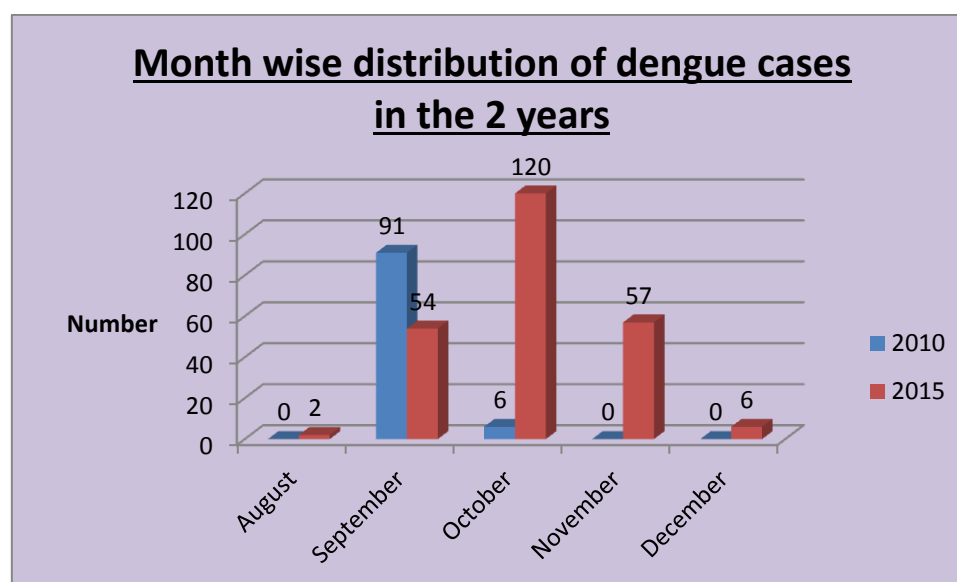
In both the years males outnumbered the females being 77.3% and 70.3% respectively in 2010 and 2015. Also, the male/female ratio is greater than 1 which is 2.3 in 2010 and 3.6 in 2015.

In the year 2015, maximum (61.92%, n=148) hailed from district Nainital inclusive of Ramnagar area, Haldwani block, Lalkuan followed by 24.27% (n=58) from US nagar while 6.28% (n=15) were from adjoining state from UP inclusive of Bareilly, Bijnaur, Pilibhit, Rampur

area and 1 case was from Nepal state. The minimum number of cases were from Almora with 3.76% (n=9), Pithoragarh with 1.67% (n=4), both Bageshwar and Champawat each with 0.84% (n=2) and only 0.42% (n=1) case was from district Chamoli.

In the year 2010 no case was reported from the districts Bageshwar, Chamoli and Pithoragarh. As in 2015 the maximum cases were from the district Nainital because of outbreak occurred around the forest compound area of Ramnagar area and the number is 76.29% (n=74).

In the study some dengue cases found in army personnel, forested area as Ramnagar area of district Nainital is a forested area besides the usual urban/rural distribution of dengue cases.



In the year 2010 cases occurred in the months September & October whereas in the year 2015 cases reported in the months of August, September & October in increasing trend and also in

November & December in decreasing trend. Thus, dengue cases occurred more in the monsoon period.

Table: Overall and sex wise mean age

Total dengue cases (Age)	2010		2015	
	Mean \pm SD	Range (in years)	Mean \pm SD	Range(in years)
Overall (n=97 in 2010 & n=239 in 2015)	30.48 \pm 13.03	7 to 65 years	32.26 \pm 12.04	16 to 75 years
Male (n=77 in 2010 & n=168 in 2015)	29.6 \pm 12.31	7 to 65 years	32.05 \pm 12.13	16 to 75 years
Females (n=22 in 2010 & n=71 in 2015)	33.50 \pm 15.15	15 to 63 years	32.77 \pm 11.90	17 to 60 years

In 2015 the average age of the dengue cases studied was 32 years having age range of 16 to 75 years. The males and females were having similar mean age. While in 2010 the average age of

dengue case was almost the same as in 2015 with young children affected as the age range is from 7 to 65 years unlike in 2015.

Table-2 : Serologically confirmed dengue cases and their clinical type

Rapid test/ELISA results	2010	2015
	Number (%)	Number (%)
NS1 + and IgM +	76 (78.35%)	225 (94.14%)
NS 1 – and IgM+	3 (3.09%)	14 (5.86%)
NS+ and IgM -	18 (18.56%)	0
Total	97	239 (100.0%)
Type of dengue cases	2010	2015
	Number (%)	Number (%)
Dengue fever	78 (80.41%)	204 (85.36%)
Dengue fever with bleeding	7 (7.23%)	5 (2.09%)
DHF-I	0 (0%)	18 (7.53%)
DHF-II	12 (12.36%)	4 (1.67%)
DSS	0 (%)	8 (3.25%)
Total	97 (100.0%)	239 (100.0%)

All the 239 cases included in the study were serologically confirmed dengue cases with IgM positivity. Almost in 94.14% cases (n=225) in the

2015 and 78.35% in 2010 the perfect positive correlation was observed between the NS 1 and IgM positivity. Only 5.86% (n=14) cases were found to be negative on NS 1 but positive on using IgM ELISA test kits. None of the case was found to be false positive on rapid test in 2015 unlike 18.56% in 2010.

In the year 2015 the percentage of DHF-I and DHF-II cases in the study was 7.53%(n=18) and 1.67% (n=4) respectively with a total of 9.2% while the DSS cases were 3.25%(n=8). Whereas the proportion of DHF cases in 2010 was 12.36% higher than in 2015 but no severe DSS was found. Bleeding manifestation in the form of mucosal bleed/epitaxis/hemetemesis or malaena were present in the DHF-II cases. Also, the raised hematocrit value is >20% was found in the DHF and DSS cases.

Table-3 : Period of hospital stay of dengue cases from the date of admission in both the year

Period of hospital stay from the date of admission	2010	2015	Overall mean period of hospital stay from date of admission (in days)
	Number (%)	Number (%)	
Same day of admission (No stay)	0 (%)	4 (1.67%)	3.51 ± 1.80 (in 2015)
1 day	2 (2.06%)	27 (11.3%)	
2 day	11 (11.43%)	43 (17.99%)	
3 day	40 (41.24%)	57 (23.85%)	
4 day	34 (35.05%)	43 (17.99%)	
5 day	9 (9.28%)	42 (17.57%)	3.41 ± 0.92 (in 2010)
6 day	1 (1.03%)	10 (4.18%)	
7 day	0 (0%)	8 (3.35%)	
9 day	0 (0%)	1 (0.42%)	
10 day	0 (0%)	2 (0.84%)	
13 day	0 (0%)	1 (0.42%)	
14 day	0 (0%)	1 (0.42%)	
Total	97 (100.0%)	239	

Majority of the dengue cases had stayed for 3 days of admission in 23.85% (n=57) followed by 4 day and 2 day of admission, each with 17.99% (n=43), 5 day of admission in 17.57% (n=42), 1 day of admission in 11.3% (n=27). There were few dengue cases who stayed for 6 days of admission in 4.18% (n=10) followed by 7 days of admission in 3.35% (n=8). Least percentage of patients had

stayed for 9 days or 13 days or 14 days each with 0.42% (n=1) and 0.84% (n=2) had stayed for 10 day of admission.

As the severity and number of dengue cases with DSS was less in the year 2010 the period of stay in the hospital was comparatively lesser than in 2015.

Table-4 : Clinical and investigation findings of dengue cases in 2015

Specific Clinical /Investigation findings	Number (n=239)	Percentage
Pleural effusion	19 (10+7+2)	7.95%
Ascites	13	5.44%
Hepato/Splenomegaly	7	2.93%
Seizures/altered sensorium/encephalopathy	3	1.26%
Extensive rashes	1	0.42%
Hypotension (due to DHF/DSS)	10	4.18%
INVESTIGATION FINDINGS		
Proteinuria increased/urinary cast	2	0.84%
Total leucocyte count	Number (n=239)	Percentage
Leucopenia (<4000cells/mm)	109	45.61%
No leucopenia	130	54.39%
Platelet count	Number (n=239)	Percentage
≤ 50000	159	66.53%
50000 -1lakh	56	23.43%
>1lakh	24	10.04%
SGOT/SGPT ratio	Number	Percentage
<2	153	64.01%
≥2	84	35.15%
Co-morbid conditions	Number (n=239)	Percentage
CAD (Coronary artery disease)	1	0.42%
COAD (Chronic obstructive airway disease)	1	0.42%
Acalculous cholecystitis	1	0.42%
ESR increased	1	0.42%
DM	5	2.09%
HTN	3	1.26%
HBsAg/HCV +	3	1.26%
CML	2	0.84%
HIV+	1	0.42%
Seizure disorder	1	0.42%
Scrub typhus (8 months pregnancy)	1	0.42%
MODS (Multiple Organ Dysfunction Syndrome)	1	0.42%
Malaria	1	0.42%

Among the clinical/investigation findings specific to dengue disease were pleural effusion in 7.95%, ascites in 5.44%, hepato/splenomegaly in 2.93%, neurological manifestations in 1.26% cases. Out of 19 pleural effusion cases in 10 cases there was right pleural effusion, 7 were having bilateral pleural effusion and 2 were having left pleural effusion. Hypotension was revealed in 4.18%. In 0.84% serum protein level was raised and in only 1 case extensive rashes was present. Raised SGOT/SGPT levels ≥ 2 was seen in 35.15% in the form of symptomatic/asymptomatic hepatic involvement most likely due to dengue or may be other co-incidental health conditions. There were 2 cases where the blood serum amount inadequate for finding the ratio of SGOT/SGPT.

While the co-incidental findings not specific to dengue disease was also found in the cases. One female pregnant case was having scrub typhus/typhoid fever. The 2 patients were of CML, viral hepatitis positive cases were 3 with 1 HIV positive case was also found. Diabetes was observed in 5 cases and hypertension was seen in 3 cases. Other less frequency of coincidental health conditions were CAD, MODS, Malaria.

Leucopenia was found in 45.61% (n=109). The platelet count ≤ 50000 was present in 66.53% (n=159) while between 50000- 1lakh was observed in 23.43% (n=56) cases.

Table-5 : clinical and investigation findings of dengue cases in 2010

	Number	Percentage
GIT manifestation	22	22.68%
General weakness/bodyache/headache	19	19.59%
Retroorbital pain	16	16.49%
Rash	13	13.40%
Altered sensorium	1	1.03%
MP+	1	1.03%
Pregnant woman/amenorrhoea for 3 months	1	1.03%
Bleeding manifestations	19	19.59%
INVESTIGATION FINDINGS		
Total leucocyte count	Number	%
Leucopenia (<4000cells/mm)	49	50.52%
No leucopenia	48	49.48%
Platelet count	Number	%
<50000	23	23.71%
50000-1lakh	42	43.30%
>1lakh	32	32.99%
SGOT/SGPT ratio		
<2	72	74.22%
≥2	15	14.55%

The gastrointestinal manifestation was seen more in 22.68% followed by weakness/bodyache/headache in 19.59%. The bleeding manifestation accounting for 19.59% was reported in DF w bleeding and in DHF cases in the form of mucosal bleeding/epistaxis/hemetemesis/malena/petachie or purpura.

One case was found positive for malarial parasite and also one pregnant female with 3 months amenorrhoea was observed with dengue infection. Leucopenia was found in 50.52% whereas platelet count <50000 was present in 23.71%

Table-6 Fatal Outcome of dengue cases in both the years

Fatal Outcome	2010	2015
	Number (%) n 97	Number (%) n 239
Expired	2 (2.06%)	3 (1.25%)

The remaining patients in both the years were either got LAMA, discharge on patient request and discharged satisfactorily. The case fatality ratio is $3/239 \times 100 = 1.25\%$ in the 2015 and $2/97 \times 100 = 2.06\%$ in the 2010.

Discussion

The Directorate of National Vector Borne Disease Control Program (NVBDCP) is the central nodal agency for the prevention and control of vector borne diseases, that is, malaria, dengue, lymphatic filariasis, kala-azar, Japanese encephalitis, and chikunguinea in India. There has been a surge in dengue cases in the country in 2012 when as many as 50,222 cases were reported against 18,860 in 2011 as dengue is emerging as a major public health problem in India. In view of upsurge and geographical spread of dengue to newer areas, a mid-term plan has been developed by Government of India for prevention and control of dengue. Field visits are carried out to assess the preparedness and to provide technical guidance to states. Training is also imparted to clinicians on case management as per Government of India guidelines and to other health care functionaries on program activities. For augmenting diagnostic facilities, the number of Sentinel Surveillance Hospitals (SSHs) with laboratory support has been increased to 347 across the country from 110 and linked with 14 apex referral laboratories with advanced diagnostic facilities for back up support for dengue across the country.¹² Our tertiary care hospital that is STH is one of the sentinel site for dengue outbreak cases.

In the current study, the male/female ratio is greater than 1 which is 2.3 in 2010 and 3.6 in 2015 with maximum cases of 38.14% (n=34) in the age group 21-30years. The sex ratio finding also supports with the study done in delhi by NH ahmed et al¹³ on the 1,700 serologically confirmed dengue cases, where the male-to-female ratio was 1.6:1. More males cases is due to their outdoor activity than females. In the same study in delhi, the largest number of positive samples (30.8%) was from the age-group 21-30 years which is lower than the present finding of 38.14% (n=34). The difference may be due to different sample size taken in different studies. The youngest patient was a 1-month-old male child and the oldest was an 87-year-old male patient in a study conducted in delhi. The age

range of the studied subjects of the present study was from 16 to 75 years. Although in the study younger child population upto 5 years and between 5-15 years was not found to be affected with dengue infection. Unlike the findings of the delhi study the present study showing shift of dengue infection in young adult population. Gupta et al¹⁴ and Chakravarti & Kumari¹⁵ also reported maximum cases in the age group 21-30 years with male preponderance.

In a study by NH ahmed et al in delhi¹³, they have found that 10.3% of 1700 were DHF patients and the mortality in serologically confirmed dengue fever cases were 0.06% with DSS cases of 1% . This finding is in accordance with the results of the present study where the frequency of DHF cases in 2015 was 9.2% with slightly higher percentage of DSS cases of 3.25%.

Ascites and pleural effusion from capillary leak syndrome are one of those features, more and more reported in recent years of outbreaks, by the help of technological advances like ultrasonography. Sanjay Kumar Mandal et al in eastern India have reported 3rd space collection in the form of ascites and pleural effusion in 8.1% and 18.9% of cases.¹⁶ In the study by Singh NP et al¹⁷, ascites was in 1.08% and pleural effusion was also in 1.08% cases. Our findings of ascites and pleural effusion percentage is of 5.44% and 7.95% in 2015 in the present study.

Low leukocyte count in DF, may be due to virus induced inhibition/destruction of myeloid progenitor cells. Sanjay Kumar Mandal et al in eastern India only 29.73% cases had leukocyte count below 4000/cmm¹⁶. But in study of Itoda et al¹⁸, leucopenia was detected in 71% cases, while Tripathi AK et al¹⁹, reported leucopenia in 90%. Mittal H et al²⁰, found leucopenia in 19.2% cases and in Bangladesh based study by Rahim MA²¹ detected it in only 4.1% cases. Our study results of leucopenia with 45.61% in 2015 and 50.52% in 2010 is in contrast with findings reported in other south asian countries of japan and Bangladesh and also with above quoted indian author studies. This

may be due to regional differences, type of study subjects (children/adults) in various studies.

Platelet count of 50000 and 50000-1lakh was seen in 66.53% and 23.42% respectively in 2015 and 23.71% & 43.30% respectively in 2010 while the study from eastern part of India by Sanjay Kumar Mandal et al have found out of 74 patients, 28 (37.84%) had platelet count below 50,000/cumm of blood and the rest 46 patients (62.16%) had more than 50,000/cumm of blood.¹⁶

In this study we have presented the findings of different co-incidental findings of scrub typhus, malarial and viral hepatitis and pregnant women cases also among dengue cases. Also, the average period of hospital stay of dengue patients was of 3 days as revealed from the study.

Only 3 deaths occurred in the reported dengue cases in this study giving case fatality ratio of %. Whereas in a study in AIIMS delhi by NH ahmed et al¹³ observed At AIIMS, with only one death, the mortality was even lower (0.06%).

Dengue fever is a re-emerging public health problem with two-fifths of the world population being at risk of infection. Till now, dengue fever was believed to be caused by four different serotypes. The fifth variant DENV-5 has been isolated in October 2013. This serotype follows the sylvatic cycle unlike the other four serotypes which follow the human cycle. The likely cause of emergence of the new serotype could be genetic recombination, natural selection and genetic bottlenecks. There is no indication of the presence of DENV-5 in India. Recent clinical trials with the promising Chimerivax tetravalent vaccine suffered a setback. Discovery of DENV-5 and more such sylvatic strains in future may further impede the Dengue Vaccine Initiative. Integrated Vector Management holds the key to sustainable dengue control. Further epidemiological and ecological studies are needed to detect additional sylvatic dengue strains.²²

Limitation

The detection and serotypic characterisation of dengue virus by the RT-PCR was not performed.

The study does not give information of primary and secondary dengue cases.

Conclusion and Recommendation

In the study the pattern of dengue cases in the two outbreaks in different years was seen more in the active age group and males having more outdoor activity were more affected with dengue infection. Certain concomitant conditions like hepatitis, scrub typhus, malaria infection was also observed in dengue cases. In the Uttarakhand inspite of high altitude state dengue cases were observed in the form of outbreaks as the aedes mosquito being cold blooded is thriving in the high altitude state also. Thus because of persistent ecological changes, travel pattern, changing lifestyle pattern, army personnel and forested area should also be taken care of by the policy makers while devising prevention/control guidelines for the emergency preparedness of dengue outbreaks. Public awareness and public education regarding dengue is of utmost importance for prevention as well as for treatment of dengue fever.

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