Research Article

Studies on Symptomatic Profiles of Dengue Fever (DF) vis-à-vis Non-Dengue Fever (NDF) in District Dehradun, Uttarakhand

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Abstract

Dengue is considered to be common in most tropical and subtropical regions. The unplanned development of Dehradun city along with increasing circumference of slum areas has resulted in proportional increase of dengue prevalence. Dengue detection by conducting molecular and virological tests is complex, tedious to perform, and is less feasible for routine laboratory practices. Hence, this study was sought to describe the clinical, laboratory and ultrasonic manifestation of dengue fever based on two year's (2013 and 2014) record in order to classify the features between DF and NDF. Out of a total of 15,556 cases (8253 cases in 2013 and 7303 cases in 2014) of suspected dengue fever, 242 cases (122 in 2013 and 120 in 2014) were reported positive confirming 1.56% serologically by ELISA, which were classified as DF cases and rest as NDF cases. The significant features in DF cases were myalgia, body ache, nausea, retro-orbital pain, skin rash, leukopenia, ALT <50, splenomegaly and hepatomegaly.

The sensitivity was found highest in myalgia (91.32%), followed by body ache (88.02%) and nausea (81.82%), whereas highest specificity was found in skin rash (97.56%), trailed by leukopenia (96.63%) and hepatomegaly (96.06%). These predictive values can help the clinician to be more confident that a patient lacking these features does have the disease because of high negative prediction values. Changing characteristics of the disease deserve serious research attention, especially in shifts in modal age, rural spread, social and biological determinants of race; and sex related susceptibility have major implications for health service planning and control strategies.

Keywords: DF, NDF, Dehradun, Uttarakhand.

Introduction

Dengue, an arthropod-borne acute febrile-viral disease, is now-a-days one of the most significant concerned epidemics because it is associated with high rates of morbidity and mortality.[1] The etiologic of dengue is the dengue virus (DENV), which belongs to family *Flaviviridae* and genus *Flavivirus* consisting of four serotypes (DENV-1 to DENV-4). Compared to nine reporting countries in the 1950s, today the geographic distribution includes more than 100 countries, notably in South-East Asia with an estimation of 2.5 billion people bearing a high risk of DF/DHF and cyclical epidemics.[2,3] Globally, every year, an estimated 50 million dengue infections occur; half a million DHF cases require hospitalization with over 20,000 deaths.[4]

Dengue is emerging as a major public health problem in India. Dengue infection has been known to be endemic in India for over two centuries as a benign and self-limited disease.[5] Since the first epidemic in Kolkata during 1963-64, many places in India have been experiencing dengue infection.[6] One of the largest outbreaks in North India occurred in Delhi and adjoining areas in the year 1996.[7,8] Studies on clinical and serological profiles have been reported from different dengue epidemic areas of India [5,9-13] and have also been quoted across the world.[14-19]

Looking at the highly complex pathophysiological, economic and ecological problems of the dengue patients, it is needed to know the early features that distinguish DF from other febrile illnesses. Serological and virological diagnosis of dengue requires long, intensive and tedious work with advanced laboratory setups which are often not available in distant remote areas of district Dehradun, where dengue had put its epidemic claws since 2006 (unpublished data). Thus, this study sought to describe the clinical, laboratory and ultrasonic manifestation of dengue fever based on two years' (2013 and 2014) record in order to simplify the classification between DF and febrile illness.

Materials and Methods

Study Area

The study was performed based on clinical data of the consecutive years 2013 and 2014 procured from the Chief Medical Office, Dehradun, of both suspected and confirmed dengue cases of district Dehradun.

Statistical Analysis

In order to compare DF and NDF, crude odds ratios (ORs) were calculated for determining the magnitude of various risk factors. Further, Chi-square test was performed and value of significance used for all statistical tests was p <0.0001. The tests that were significant in χ^2 were further analyzed for sensitivity, specificity and predictive values.[18] Data were analyzed in SPSS (version 17.0).

Results

Out of a total of 15,556 cases (8253 cases in 2013 and 7303 cases in 2014) of suspected dengue fever, 242 cases (122 in 2013 and 120 in 2014) were reported as positive being classified as dengue fever (DF) cases and the rest as non-dengue fever (NDF) cases. Month-wise distribution that indicates the seasonality of both suspected and confirmed cases is represented in Fig. 1.

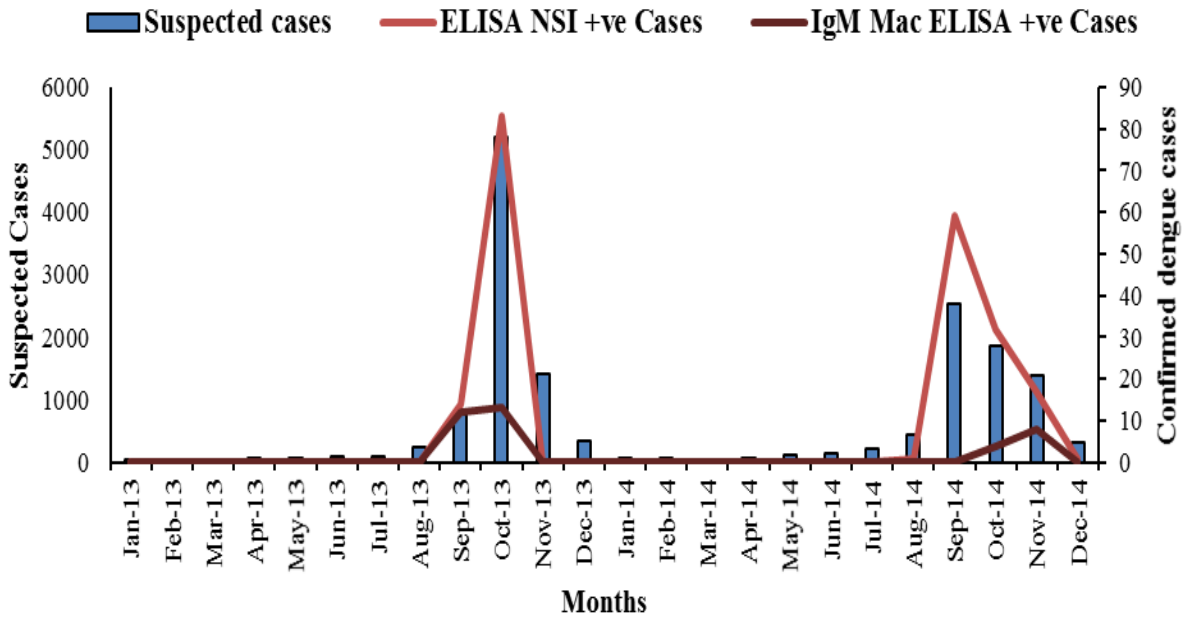

Figure 1.Month-Wise Distribution of Suspected and Confirmed Dengue Cases in District Dehradun, 2013 and 2014

The highest number of DF cases accounting 40.16% (49 cases) was encountered among the age group 31–50 years in 2013, whereas in 2014 it happened to hover around the age group of 11–30 years with 35% (42 cases). However, in both years the lowest number of cases was accounted from ≥10 age group. In demographic distribution, men were found more largely infected than women; however in performing a χ^2 test (2×2) p-value suggests no significant demarcation of the disease among male and female, whereas in case of age distribution, χ^2 test (5×4), significant value of p (<0.0001) was estimated. The detail of demographic distribution is represented in Table 1.

Table 1.Demographic Distribution of DF and Non-DF Cases in District Dehradun, 2013 and 2014

Demographic Characteristics	DF		NDF		*p* value
	2013	2014	2013	2014	
Sex, n (%)					0.000926
Male	81 (66.40)	73 (60.83)	6033 (74.20)	5171 (71.99)	
Female	41 (33.60)	47 (39.17)	2098 (25.80)	2012 (28.01)	
Age in years, n (%)					< 0.0001*
≥ 10	02 (1.64)	01 (0.83)	197 (2.42)	113 (1.57)	
11–30	31 (25.41)	42 (35.0)	2370 (29.15)	2687 (37.41)	
31–50	49 (40.16)	36 (30.0)	3016 (37.1)	2713 (37.77)	
51–70	35 (28.69)	36 (30.0)	1758 (21.61)	1375 (19.14)	
≤71	05 (4.10)	05 (4.17)	790 (9.72)	295 (4.11)	

*significant *p*-value <0.0001

The most common clinical symptoms among DF cases were fever (100%), myalgia (91.32%), body ache (88.02%), nausea (81.82%) and retro-orbital pain (56.20%). Among the clinical symptoms accounting, significant *p*-values were found in low ORs (in CI 95%), i.e., nausea (2.4518), followed by body ache (2.8684), myalgia (4.8059), retro-orbital pain (8.0866) and skin rash (16.6316) in succession (Table 2).

On considering the laboratory parameters, leukopenia (n=79; 32.64%) and alanine aminotransferase <50 (n=115; 47.52%) were significantly associated with DF (*p* <0.0001). Both parameters were associated significantly in high ORs values (13.8993 and 18.4889 respectively) as depicted in Table 2.

In ultrasonic manifestation, a total of 441 patients were reported of splenomegaly, out of which 43 (17.27%) reported positive with DF, whereas in hepatomegaly out of 716 patients only 113 (46.70%) were positive with DF. Both these parameters with high ORs values were found to be significantly associated with DF (*p* <0.0001) (Table 2).

Table 2.Epidemiology Characteristics of DF and Non-DF Cases in District Dehradun, 2013 and 2014

Characteristics	DF	NDF	Odds Ratio (95% CI)	*p* value
Clinical Symptoms				
Fever	242 (100.00)	14007 (91.47)	45.20 (2.82 to 725.19)	0.0071
Myalgia	221 (91.32)	10513 (68.65)	4.8059 (3.07 to 7.53)	< 0.0001*
Body ache	213 (88.02)	11013 (71.91)	2.8684 (1.94 to 4.23)	<0.0001*
Nausea	198 (81.82)	9913 (64.73)	2.4518 (1.77 to 3.40)	<0.0001*
Vomiting	53 (21.90)	5137 (33.54)	0.5556 (0.41 to 0.75)	0.0002
Retro-orbital pain	136(56.20)	2097 (13.70)	8.0866 (6.25 to 10.47)	<0.0001*
Itching	78 (32.23)	5837 (38.12)	0.7722 (0.59 to 1.01)	0.0621
Abdominal pain	103 (42.56)	8314 (54.29)	0.6239 (0.48 to 0.81)	0.0003
Skin rash	71 (29.34)	373 (2.44)	16.6316 (12.38 to 22.34)	<0.0001*
Loose motion	37 (15.29)	3497 (22.84)	0.6099 (0.43 to 0.87)	0.0059
Laboratory Parameters				
Thrombocytopenia	25 (10.33)	1211 (7.90)	1.3417 (0.88 to 2.04)	0.1683
Requirement of PRP	27 (11.16)	1155 (7.54)	1.5395 (1.03 to 2.31)	0.0366
Leukopenia	79 (32.64)	516 (3.37)	13.8993 (10.48 to 18.44)	<0.0001*
ALT <50	115 (47.52)	715 (4.67)	18.4889 (14.21 to 24.06)	<0.0001*
AST <50	110 (45.45)	8456 (55.22)	0.6759 (0.52 to 0.87)	0.0026
Ultrasonic Manifestation				
Splenomegaly	43 (17.77)	398 (2.60)	8.0981 (5.74 to 11.43)	<0.0001*
Thickened gall bladder	21 (8.68)	1103 (7.20)	1.2243 (0.78 to 1.92)	0.38
Third space loss	19 (7.85)	998 (6.52)	1.2222 (0.76 to 1.96)	0.4055
Hepatomegaly	113 (46.70)	603 (3.94)	21.3704 (16.39 to 27.86)	<0.0001*
Total	242	15314		

*significant *p*-value <0.0001, PRP= Platelet rich plasma, ALT= Alanine aminotransferase, AST= Aspartate aminotransferase

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The significant symptoms in dengue cases were myalgia, body ache, nausea, retro-orbital pain, skin rash, leukopenia, ALT <50, splenomegaly and hepatomegaly. The sensitivity, specificity, like hood and predictive values of these parameters in dengue diagnosis, is shown in Table 3. The sensitivity was found highest in myalgia (91.32%), followed by body ache (88.02%) and nausea (81.82%), whereas the lowest was found with skin rash (29.34%). In case of specificity highest percentage was found in skin rash (97.56%), trailed by leukopenia (96.63%) and hepatomegaly (96.06%) while the lowest was recorded from body ache (28.09%). Likehood ratio positive values {sensitivity/(1-specificity)} were much higher than negative values {(1-sensitivity)/specificity}. The calculated predictive values of all the parameters of dengue fever were found to be inclined highly towards negative prediction values. The overall disease prevalence was found to be 1.56% confirmed serologically by ELISA test (Table 3).

Table 3.Sensitivity, Specificity, Likehood Ratio Predictive Values of Certain Parameters and Disease Prevalence of Dengue Cases in District Dehradun, 2013 and 2014

Clinical Features	Sensitivity (%)	Specificity (%)	Likehood Ratio		Predictive Values		Disease Prevalence (%)
			Positive	Negative	Positive (%)	Negative (%)	
Myalgia	91.32	31.35	1.33	0.28	2.06	99.56	1.56
Body ache	88.02	28.09	1.22	0.43	1.90	99.33	
Nausea	81.82	35.27	1.26	0.52	1.96	99.19	
Retro-orbital pain	56.20	86.31	4.10	0.51	6.09	99.20	
Skin rash	29.34	97.56	12.05	0.72	15.99	98.87	
Leukopenia	32.64	96.63	9.69	0.70	13.28	98.91	
ALT more than 50	47.52	95.33	10.18	0.55	13.86	99.14	
Splenomegaly	47.52	95.33	10.18	0.84	9.75	98.68	
Hepatomegaly	46.69	96.06	11.86	0.55	15.78	99.13	

Discussion

The epidemiology of DF/DHF is complex involving host, viral and vector status that are further influenced by demographic, economic, behavioral and varied societal factors.[3] The present study highlighted the findings of the research in southern lowlands of Nepal[18] that maximum frequency of dengue cases were recorded in between the months of August-November (monsoon-post-monsoon period), suggesting the fact of prevalence of optimum conditions (precipitation) for mass breeding and propagation of vectors influencing the transmission of virus.[11] Dengue-specific antibodies were positive in 1.56% of patients, which is comparable to other studies conducted in Delhi,[5] Chennai,[10] and Lucknow.[12]

In the present study, higher cases of infestation were found in men (though *p*-value not significant) supporting the work in Taiwan[14] and Amazonas state[20] however distinctly vary from the studies conducted in Thailand[19] and Nicaragua.[21] Almost all of these studies were hospital-based, so probably only represent those who access healthcare rather than the real infected population, suggesting gender bias is still abundant in many countries.[22]

In South-East Asian countries, where all the serotypes (DENV-1-4) are circulating, DF is typically acknowledged to be a disease of early childhood, while clinical DF in adults is rare.[23] However, current study focused on the increase of dengue incidence in older age groups; this age shift has been reported in Singapore, Indonesia, Bangladesh and Thailand.[24-26]

The clinical symptoms of the present study were most significantly associated with DF and were more or less similar with other clinical manifestations reported in different studies.[13,15] Differences in genetics related to immune response of host may play a role in severity of infection.[16] Among the laboratory parameters, thrombocytopenia and leukopenia were reported to be associated with dengue fever,[17,18] however, in the present study only leukopenia is found to be significant.[27] The value of liver enzymes AST (aspartate aminotransferase) and ALT (alanine aminotransferase) was comparable with the studies of Aikat et al.[28] suggesting liver abnormality in dengue infection along with alteration in liver functions. The results of ultrasonic manifestation were more or less similar with the findings from Delhi and Kolkata.[9]

Sensitivity for the prediction of dengue cases was high for myalgia, body ache and nausea; on the other hand skin rash had higher specificity, predicting its absence directly proportionating with no dengue infestation.

These predictive values can help the clinician to be more confident that a patient lacking these features does

have the disease because of high negative prediction values.[18] The clinical and laboratory findings are equally reliable in distinguishing dengue from other febrile illnesses at an early stage thus reducing dengue-associated morbidity and mortality; however, all febrile cases should be monitored for the development of signs and symptoms, which happen to be troublesome methods. Changing characteristics of the disease deserve serious research attention especially in shifts in modal age, rural spread, social and biological determinants of race and sex-related susceptibility have major implications for health service planning and control strategies.

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Conflict of Interest: None

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