Original Research Article

Clinical presentation and Laboratory findings in patients with dengue fever in tribal region of Adilabad

R Sridhar Reddy[1], Samala Raghuram Mohan[2], Mohd Inayatulla Khan[3], S Chandra Sekhar[4]
[1]Associate Professor, Department of Pathology, Rajiv Gandhi Institute of Medical Sciences, RIMS, Adilabad.
[2]Assistant Professor, Department of Pathology, Kakatiya Medical College, KMC, Warangal
[3]Department of Physiology, Rajiv Gandhi Institute of Medical Sciences, RIMS, Adilabad
[4]Professor and HOD, Dept of Pathology, Rajiv Gandhi Institute of Medical Sciences, RIMS, Adilabad

*Corresponding author
Dr R Sridhar Reddy
Email: rdd.sridhar@gmail.com

Abstract: Dengue is increasingly becoming a major health problem of the world. It has become as one of the disease of major concern in Tropical countries. Growing menace of Dengue has led to increase burden on the health care system in endemic areas of India. The aim of the study was to observe the clinical presentation and Laboratory findings of clinically suspected dengue cases in tribal region of Adilabad. This retrospective study was conducted in Rajiv Gandhi Institute of Medical Sciences [RIMS] Adilabad during period from 2013 to 2014 dengue active season. Adult patients with acute febrile illness were evaluated for clinical features of dengue fever, dengue hemorrhagic fever and dengue shock syndrome. Patients presenting with typical symptoms of dengue fever were evaluated. Fifty (n=50) patients of both sexes were included during the study. Out 50 cases 32 (64%) were male and 18 (36%) were female patients. 22 (44%) out of 50 were dengue suspected cases and 28 (56%) 50 were dengue proven cases. Out of 28 dengue proven cases 26 had dengue fever and 2 had dengue hemorrhagic fever. The most common clinical presentation was fever in 78.6% of patients with myalgia 50% of the patients followed by abdominal pain in 53.6% of patients, headache was reported by 39.3% of the patients and bleeding manifestation was seen in 17.8% of patients. The Laboratory findings were Thrombocytopenia in 89.3% of patient with leucocytopenia in 25% of the patients ALT was raised in 40% of cases and 28.5% cases showed NS1Ag negative and IgM positive in tests. High suspicion for Dengue should be considered in patients reporting from endemic areas of dengue infection with clinical presentation of fever with myalgia, abdominal pain and headache with bleeding manifestations. However confirmation of dengue can be done only with Laboratory findings which include NS1Ag, dengue serology IgM and IgG, thrombocytopenia, increased ALT.
Keywords: Dengue Fever, Clinical Presentation, Laboratory Findings

INTRODUCTION

Dengue is the most prevalent mosquito-borne viral infection of tropical and subtropical region which includes 100 countries. World health Organization [WHO] declares dengue and dengue hemorrhagic fever to be endemic in south Asia. They currently estimate that there may be over 50 million dengue infections worldwide every year [1]. The South Asian region of India, Indonesia, Myanmar and Thailand are at highest risk of dengue accounting for nearly half of global risk [2]. In countries like India epidemics of dengue are straining the limited resources of public health care system. Dengue virus was isolated in India for the first time in 1945. The first evidence of occurrence of dengue fever in the country was reported in 1956 from Vellore district in Tamil Nadu. The first dengue hemorrhagic fever (DHF) outbreak occurred in Calcutta (West Bengal) in 1963 [3, 4]. Many dengue cases are self-limiting but complications such as hemorrhage and shock can be life threatening [5]. Dengue is a flavivirus transmitted by the bite of Aedes Aegypti mosquito, which generally acquires the virus while feeding on the blood of an infected person and transmit the disease to another non infected person. It is primarily a day time feeder lives around human habitation. Dengue virus is a positive stranded, encapsulated RNA virus and there are four serotypes of dengue virus (DEN1-4) after an incubation period of 4-10 days, infection by 4 virus

serotypes can produce wide spectrum of illness although most infections are asymptomatic and subclinical and the recovery of infection from one serotype can confer life-long protection against that serotype but not against the other three serotypes [6]. Severe dengue infection usually occurs after a second infection with a different serotype, which is due to immune-mediated antibody-dependent enhancement (ADE) [7, 8]. WHO defined Dengue fever as acute febrile illness of 2-7 days duration sometimes with two peaks having following manifestations of abrupt onset of malaise, facial flush, myalgia, joint pains and rash hemorrhagic manifestations or leucopenia [9]. The Dengue virus infections have been categorized into three groups based on the symptoms; undifferentiated fever, Dengue Fever (DF) and Dengue Hemorrhagic Fever [DHF]. The DHF is further classified into four categories based on severity of grades with grades III and IV as Dengue Shock Syndrome [DSS] [10]. Plasma leakage, haemo concentration and abnormalities in homeostasis characterize severe dengue. Thrombocytopenia may be associated with alterations in mega karyo cytopoieses by the infection of human haematopoietic cells and impaired progenitor cell growth, resulting in platelet dysfunction (platelet activation and aggregation), increased destruction or consumption (peripheral sequestration and consumption). Haemorrhage may be a consequence of the thrombocytopenia and associated platelet dysfunction or disseminated intravascular coagulation. It is a transient imbalance of inflammatory mediators, cytokines and chemokines that occurs during severe dengue due to early heavy viral burden leading to derangement of hemocoagulation system followed by plasma leakage, shock and bleeding. Laboratory diagnosis of dengue was based on presence of NS1 Antigen and the dengue serology for the presence of IgM or IgG antibodies. With this background we tried to evaluate the clinical features and laboratory findings in patients with dengue symptoms for early management and favorable outcomes.

MATERIALS AND METHODS

The present study was conducted in Rajiv Gandhi Institute of Medical [RIMS] Adilabad a tertiary care hospital catering needs of predominantly tribal region of Adilabad district of Telangana State. Ethical Permission for the study was obtained from the Institutional Ethical Committee and all the procedures were done in accordance with declaration of Helsinki Ethical principles. The data was collected during the September 2013 to September 2014 season. Subjects reporting to RIMS hospital with signs and symptoms of

dengue fever according to WHO guide lines given below

WHO guidelines for dengue fever [11, 12]
Probable dengue
- Live or travel to dengue endemic areas
- Fever and 2 of the following criteria
- Nausea
- Rash
- Aches and Pains
- Tourniquet test positive
- Leukoplakia

With any of the following 'warning signs'
- Abdominal pains and tenderness
- Clinical fluid accumulation
- Mucosal bleeding
- Lethargy, restlessness
- Liver enlargement > 2cms
- *Laboratory findings*
- Increase in Haematocrit
- Rapid decrease in platelet count.

The data was collected from (n= 50) Adult patients age of the ranged from 18 to 60 years the mean age was 37.5 years and Females were 18 (36%) and Males were 32 (64%). Dengue fever was suspected when they showed symptoms according to WHO guidelines such patients were labeled as dengue suspected Then subjects were allowed to undergo specific dengue NS1 Ag test and dengue serology test, those who have positive dengue serology were defined as dengue proven cases. Patients with suggestive clinical features and negative for dengue serology were subjected to other tests including malarial parasites, Widal test to rule out the other possible causes. Laboratory Blood samples were collected by qualified technicians and 2ml of blood was obtained with anticoagulants and CBP including Hematocrit, Dengue serology, ALT, MP, Widal tests were performed. NS1Ag, IgM and IgG were performed by Rapid Dengue Combo (NS1 IGG/IGM) manufactured by Bio labs Diagnostics Mumbai. All the data collected was entered in Excel sheet and evaluated with SPSS version 17.

RESULTS

The table 1 showing 22 (44%) out of 50 were dengue suspected cases and 28 (56%) 50 were dengue proven cases. Out of 28 dengue proven cases 26 had dengue fever and 2 had dengue hemorrhagic fever. The common presentation in the dengue proven cases was fever in 22 (78.6%) the range of temperature was 100 °F to 105 °F during 1 to 7 days with myalgia in 50% of cases when compared with dengue suspected cases both

the presentations were found to be significant. The next common presentation was Abdominal pain and Lethargy 15 (53.6%) of cases followed by headache in 11 (39.3%) of cases Abdominal rash and bleeding manifestations 32.1% and 17.8% of cases the other recorded parameters are given in Table 1.

Table 1: Showing the Clinical presentation of the Dengue cases

Sl. No.	Clinical Presentation	Dengue Suspected (22)	Dengue Proven (28)	P Value
	Fever	14 (63.63%)	22 (78.6%)	<0.05*
	Myalgia	9 (40.9%)	14 (50%)	<0.05*
	Headache	5 (22.7%)	11 (39.3%)	<0.05*
	Vomiting	4 (18.1%)	5 (17.8%)	>0.05
	Diarrhoea	6 (27.2%)	5 (17.8%)	>0.05
	Rash	4 (18.1%)	9 (32.1%)	>0.05
	Purpura	2 (9%)	3 (10.7%)	>0.05
	Abdominal Pain	7 (31.8%)	15 (53.6%)	<0.05*
	Bleeding	2 (9.09%)	5 (17.8%)	>0.05
	Hepatomegaly	3 (13.6%)	5 (17.8%)	>0.05
	Splenomegaly	3 (13.6%)	5 (17.8%)	>0.05
	Haematuria	4 (18.1%)	5 (17.8%)	>0.05
	Melena	2 (9%)	3 (10.7%)	>0.05
	Hypotension	5 (22.7%)	8 (28.5%)	>0.05
	Cold clammy extremities	2 (9)	3 (10.7%)	>0.05
	Oliguria	1 (4.5%)	5 (17.8%)	<0.05*
	Pleural Effusion	0 (0)	1 (3.5%)	>0.05
	Lethargy	11 (50%)	15 (53.6%)	>0.05

* Significant

50 patients were included in the study with typical features of dengue fever. Age of the patients ranged from 18 to 60 years the mean age was 37.5 years. (64%) were male and 18 (36%) were female patients shown in the figure 1.
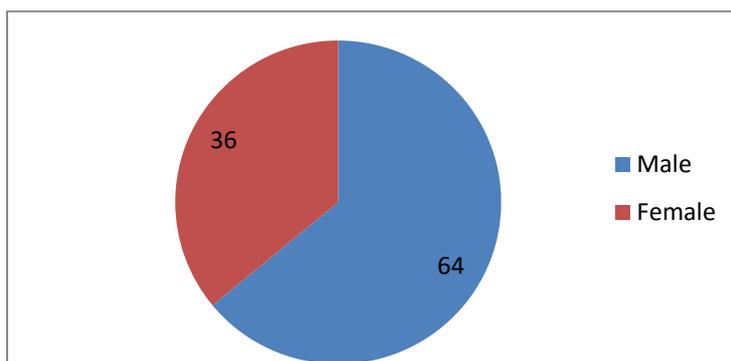
Fig 1: sex distribution of Dengue Fever Cases

The mean platelet count on 1st day was less than 1.5 lakhs/mm^3 in 25 (89.3%) of the dengue proven cases and the platelet count keep on falling till 4th and 5th day when the platelet count reduced to less than 50000/mm3 in 15 (53.6%) of cases and in 10 cases it reduced further to less than 20,000/mm^3 then slowly started increasing. Alanine aminotransferase (*ALT*) enzyme was found to increase in 11(39.3%) of the dengue proven cases. NS1Ag test was performed in all the cases None was found to be positive in suspected Dengue cases and in dengue proven cases 13 (46.4%) were found to be positive. NS1 Ag assay is considered as a useful early diagnostic marker in acute phase illness in primary and secondary dengue infection.

Dengue serology for detection of IgM and IgG was performed in patients where NS1Ag was found to be negative, 15 (53.6%) patients showed IgM positive and 7(25%) showed IgG positive.

Table 2: Showing Laboratory findings in Dengue fever cases

SL. No	Laboratory Finding	Dengue Suspected (22)	Dengue Proven (28)	P values
1.	Thrombocytopenia PLC < 1.5 Lakhs/mm^3	10 (45.5%)	25 (89.3%)	<0.05*
2.	Leucopenia TLC < 4000/mm3	3 (13.6%)	7 (25%)	>0.05
3.	Anemia Hb <10gm/dl	5 (22.7%)	12 (42.8%)	>0.05
4.	PLC < 50,000/mm3	4 (18.2%)	15 (53.6%)	<0.05*
5.	PLC < 20,000/mm3	0 (0)	10 (35.7%)	<0.05*
6.	ALT >40 IU/L	5 (22.7%)	11 (39.3%)	<0.05*
7.	NS1Ag Positive	0 (0%)	13 (46.4%)	<0.05*
9.	IgM positive	0 (0%)	8 (28.5%)	<0.05*
10.	IgG positive	0(0%)	7 (25%)	<0.05*

* Significant

DISCUSSION

Recent epidemics have shown that dengue virus is showing variable presentation. In many cases it may be subclinical and asymptomatic where as in others it may have severe manifestations. The symptoms depend on the age of the patient, immune status of the host and type of virus strain [13, 14]. We in the present study tried to evaluate the clinical presentation of dengue fever in this region, the reason for conducting such a study was during dengue season every year from September to December number of tests are ordered for suspected dengue fevers most of them eventually come out negative. This cause additional burden on the Laboratory with already limited resources, therefore treating doctors should be judicious in ordering dengue tests and they should have updated knowledge of the dengue fever presentations as per WHO criteria. Although non-specific clinical features like fever, head ache, myalgia and general malaise may develop in various other types of viral illnesses and it is sometimes difficult to diagnose mild dengue infection clinically alone. A definitive diagnosis always requires virus isolation and serology [15, 16]. In one study by AH Khan *et al*; reporting the frequency and clinical presentation of dengue fever in tertiary care hospital found that fever associated with chills and rigors, body aches, bone pain, headache, myalgia, rash and low platelet counts Leucocytopenia and increased ALT with hemorrhagic manifestations were important clinical parameters for probability of dengue fever [17]. We in the present study found fever with myalgia; abdominal pain and headache with bleeding manifestations are important signs and symptoms of dengue they were found to be present in most of the proven dengue cases. Some studies have shown that platelet count less than 50,000/mm3 elevated ALT levels can predict spontaneous bleeding [18]. In one study by AM Khazindar *et al.;* [11] proved that thrombocytopenia is the most common hematological parameter noted they reported in 58.8% of patients such results agree with our findings. They also reported that Abnormal liver functions with increase in tranaminase levels were associated with dengue fever which is again in agreement with our observations in the present study 53.6% of patients were having platelets count less than 50,000/mm3. The incidence of bleeding manifestations was found in few cases in this study Table 1. In a study by Gouber S *et al.;* [19] concluded that there was minor statistical difference in the incidence of bleeding manifestations and thrombocytopenia, indicating poor association of thrombocytopenia with bleeding, It is also in agreement in our observations, Although 53.6% of cases were having platelet counts less than 50,000/mm3 frank bleeding were seen in 5 (17.8%) of proven dengue cases. In a study by Irfan A *et al.;* found that clinical symptoms like fever headache, myalgia and rash were important clinical parameters for diagnosis of dengue fever [20]. The laboratory features that are highly predictive of dengue were decreased platelet count and increased serum amiotransferases. These findings are similar to our observed laboratory results where we found that decreased platelet count and increased transaminase levels were significantly associated with proven dengue cases. In final conclusion the best markers for dengue infection is Dengue serology including NS1Ag the presence NS1Ag positivity in patient is an early marker of dengue this can substantially reduce the hospital stay of the patients and produce better overall treatment outcome.

CONCLUSION

High suspicion for Dengue should be considered in patients reporting from endemic areas of dengue infection with clinical presentation of fever with myalgia, abdominal pain and headache with bleeding manifestations. However confirmation of dengue can be possible only with Laboratory findings which include NS1Ag, dengue serology IgM and IgG, thrombocytopenia, increased ALT.

Conflict of Interest: Nil

Source of Support: None

Ethical Permission: Obtained

REFERENCES

1. Dengue Fever World Health Organization Fact Sheet No.117. 2009 [http://www.who.int/mediacentre/factsheets/fs117/en/]. Accessed on 10/5/2017
2. Makroo RN, Raina V, Kumar P, Kanth RK. Role of platelet transfusion in the management of dengue patients in a tertiary care hospital. Asian journal of transfusion science. 2007 Jan 1; 1(1):4.
3. Baruah K, Dhariwal AC. Epidemiology of dengue its prevention and control in India. Journal of the Indian Medical Association. 2011 Feb 1; 109(2):82-6.
4. Baruah K, Biswas A, Suneesh K, Dhariwal AC. Dengue fever: Epidemiology and clinical pathogenesis. Chapter 13, Major tropical diseases: Public health perspective. Goa: Broadway publishing House; 2014: 255–71.
5. Garg P. Utility of clinical improvement and platelet count recovery time in counseling children hospitalized with suspected dengue in a resource-poor setting. JCDR. 2008; 61:149-54.
6. Halstead SB. Etiologies of the experimental dengues of Siler and Simmons. The American journal of tropical medicine and hygiene. 1974 Sep 1; 23(5):974-82.
7. Chakravarti A, Kumaria R, Kar P, Batra VV, Verma V. Improved detection of dengue virus serotypes from serum samples-Evaluation of single-tube multiplex RT-PCR with cell culture. Dengue Bulletin. 2006; 30:133.
8. Dussart P, Labeau B, Lagathu G, Louis P, Nunes MR, Rodrigues SG, Storck-Herrmann C, Cesaire R, Morvan J, Flamand M, Baril L. Evaluation of an enzyme immunoassay for detection of dengue virus NS1 antigen in human serum. Clinical and vaccine immunology. 2006 Nov 1; 13(11):1185-9.
9. Gibbons RV, Vaughn DW. Dengue: an escalating problem. BMJ: British Medical Journal. 2002 Jun 29; 324(7353):1563.
10. WHO. Dengue haemorrhagic fever: diagnosis, treatment, prevention and control, 2nd ed. Geneva, World Health Organization, 1997.
11. Ayyub M, Khazindar AM, Lubbad EH, Barlas S, Alfi AY, Al-Ukayli S. Characteristics of dengue fever in a large public hospital, Jeddah, Saudi Arabia. J Ayub Med Coll Abbottabad. 2006 Apr; 18(2):9-13.
12. Phuong HL, de Vries PJ, Nga TT, Giao PT, Hung LQ, Binh TQ, Nam NV, Nagelkerke N, Kager PA. Dengue as a cause of acute undifferentiated fever in Vietnam. BMC Infectious Diseases. 2006 Jul 25; 6(1):123.
13. Shah I, Deshpande GC, Tardeja P. Outbreak of dengue in Mumbai and predictive markers for dengue shock syndrome. Journal of Tropical Pediatrics. 2004 Oct 1; 50(5):301-5.
14. Chadwick D, Arch B, Wilder-Smith A, Paton N. Distinguishing dengue fever from other infections on the basis of simple clinical and laboratory features: application of logistic regression analysis. Journal of Clinical Virology. 2006 Feb 28; 35(2):147-53.
15. Diaz-Quijano FA, Villar-Centeno LA, Martinez-Vega RA. Complications associated to severe thrombocytopenia in patients with dengue. Revista medica de Chile. 2006 Feb; 134(2):167-73.
16. Martínez-Vega RA, Diaz-Quijano FA, Villar-Centeno LA. Low concordance between early clinical suspicion of dengue and its serological confirmation. Revista medica de Chile. 2006 Sep; 134(9):1153-60.
17. Khan AH, Hayat AS, Masood N, Solangi NM, Shaikh TZ. Frequency and clinical presentation of dengue fever at tertiary care hospital of Hyderabad/Jamshoro. JLUMHS. 2010 May; 9(2):88-94.
18. Lin SF, Liu HW, Chang CS, Yen JH, Chen TP. Hematological aspects of dengue fever. Gaoxiong yi xue ke xue za zhi= The Kaohsiung journal of medical sciences. 1989 Jan; 5(1):12-6.
19. Gomber S, Ramachandran VG, Kumar S, Agarwal KN, Gupta P, Dewan DK. Hematological observations as diagnostic markers in dengue hemorrhagic fever--a reappraisal. Indian pediatrics. 2001 May; 38(5):477-81.
20. Arshad I, Malik FA, Hussain A, Shah SA. Dengue fever; clinico-pathologic correlations and their association with poor outcome. Professional Medical Journal. 2011 Jan 1; 18(1).