www.jmscr.igmpublication.org

Impact Factor 3.79
Index Copernicus Value: 5.88
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: http://dx.doi.org/10.18535/jmscr/v4i1.33

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Typical and Atypical manifestation of Dengue Fever: A Prospective Observational Study

Authors
Kumar Rajesh[1], Rajak M.[2], Bhattiprolu K Rahi[3]
Bokaro General DNB Hospital, Bokaro
Email: *drrajeshdr@yahoo.co.in, mrazakbgh@rediffmail.com, rahikiran73@gmail.com*
Corresponding Author
Kumar Rajesh
Bokaro General DNB Hospital, Bokaro
Email: *drrajeshdr@yahoo.co.in*

Abstract

Dengue is a major health problem in many parts of India and Jharkhand state has become one of the new endemic areas for dengue. Infection with dengue virus can cause a spectrum of clinical presentation, typical and atypical with altered haematological and coagulation parameters.

Aims & Objectives: *This study was undertaken to determine the typical and atypical manifestation and haematological profile of patients of dengue admitted in tertiary care teaching hospital in Jharkhand state of India. The study was a hospital based descriptive study with prospective data collection.*

Material & Methods: *One hundred and five patients were admitted with dengue fever as per WHO diagnostic criteria from June to December 2013*

Results: *Out of 105 cases, 75cases (71.4%) had dengue fever (DF), 27 cases (25.7%) dengue hemorrhagic fever (DF) and three cases (2.8%) had dengue shock syndrome (DSS). Fever and myalgia (100%) were the most common presentation. Among three cases of DSS (2.8 %), one case (0.95%) died of ARDS and one case died of multiorgan dysfunction (0.95%). Malena was the most common bleeding manifestation (44.4%). Low platelet count of less than 100,000/cu mm was present in 47 cases (44.7%) and had poor correlativity to bleeding manifestations. Atypical manifestations included 10 cases (9.5%) of elevated CPK levels&9 cases (8.5%) of elevated LDH levels and an isolated case of hemoglobinuria.*

Conclusion: *Dengue fever has variable manifestations, sometimes puzzling to clinicians and is an important differential of fever in endemic region.*

Keywords: *Dengue fever, Dengue hemorrhagic fever, Dengue shock syndrome, Hemoglobinuria, Thrombocytopenia*

Abbreviation used: *DF - Dengue fever, DHF –Denguehemorrhagic fever, DSS - Dengue shock syndrome, AIDP - Acute inflammatory demyelinating polyneuropathy, ADEM - Acute disseminated encephalomyelitis, CPK - Creatine phosphokinase, LDH - Lactate dehydrogenase, ARDS - Acute respiratory distress syndrome.*

INTRODUCTION

Dengue made its debut as early as 1780, when Benjamin Rush described the condition as "break bone fever". Worldwide nearly two and a half billion people continue to live at risk of contracting the infection, while 50 million cases and 24,000 deaths are estimated to occur in endemic countries. This includes hospitalization of nearly half a million cases of DHF, of which 90% are children. Treated DHF/DSS is associated with a one percent mortality rate while mortality rate among untreated cases escalates to 20%[1].

Dengue fever is an arthropod borne viral fever caused by flavivirus of four serotypes DENV one to four. While dengue is endemic in more than 100 countries, most cases are reported from Southeast Asia and the Western Pacific regions. 50 million cases of dengue infection and 500,000 cases of dengue hemorrhagic fever occur in Asian countries [2].India is one of the seven identified countries in the South-East Asia region regularly reporting incidence of DF/DHF outbreaks and may soon transform into a major niche for dengue infection. Until mid-1990s, dengue was reported from only three of the four South Indian states, namely, Andhra Pradesh, Karnataka and Tamil Nadu[4]. Till date, more than 80 outbreaks have been reported from 16 States/Union Territories including Jharkhand, the largest one being in 1996, wherein a severe outbreak of DF/DHF occurred in Delhi, affecting 10,252 cases and 453 reported[3] deaths.

Dengue infections vary in severity, ranging from influenza-like self-limiting illness - dengue fever to life-threatening dengue hemorrhagic fever and dengue shock syndrome, which if left untreated are associated with mortality as high as 20%[6]. The various manifestations of dengue may not have a distinct line of demarcation[4].

At present, incidence of DF is increasing rapidly in Jharkhand but data on dengue infection is limited. Our study was intended to determine the clinical profile of dengue fever patients admitted in a tertiary care hospital in Jharkhandand to correlate these features with laboratory findings which may help us in early diagnosis and prompt management.

MATERIALS AND METHODS

Study design

The study was undertaken as a hospital-based descriptive study with prospective data collection to determine the clinical profile and outcome of all patients admitted with the diagnosis of dengue fever according to WHO criteria[7] and serologically confirmed cases.

Study area

One Hundred and five confirmed cases of dengue were admitted as inpatients in tertiary teaching hospital in Jharkhand, India from June 2013 to December 2013.

Methodology

Detailed clinical history was taken from all patients followed by thorough clinical examination of all systems with bio chemical, microbiological, hematological, radiological investigations. Serological testing was carried out using the Denguchek kit (SD Bio Line Dengue Duo). This is a rapid test, able to detect the presence of NS 1 antigen, IgM as well as IgG antibodies and results can be interpreted within 15-20 minutes. The sensitivity of the test is 92.4% and the specificity is reported to be approximately 98.4%.The tests were performed as per the kit manual. Data was collected using a pre-designed questionnaire and analyzed using Statistical Package for Social Sciences (SPSS version 17).

Inclusion criteria

All the patients admitted with symptoms suggestive of Dengue Fever as per WHO criteria and found positive with SD Bio line Dengue Duo rapid test.

Exclusion criteria

Coexistent cases of malaria, leptospirosis were ruled out by peripheral blood smear examination and serological tests. Patients with chronic kidney disease, chronic liver disease and hematological diseases were also excluded.

Limitations

Institutional data which islimited to admitted cases only.

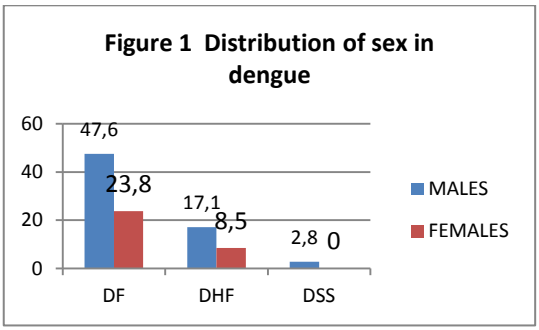
RESULTS

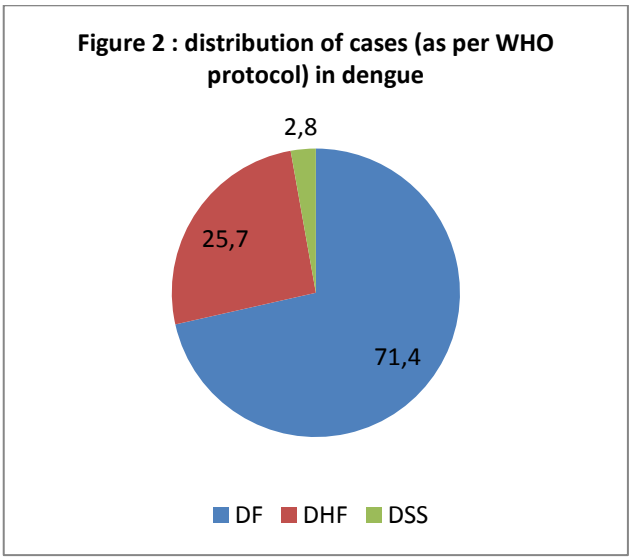
Out of 105 cases in our study, 71 cases (67.6%) were males and 34(32.3%) females. Among males, 47.6% had DF, 17.1% DHF, 2.8% DSS and among females 23.8% and 8.5% had DF and DHF respectively (Figure 1). Among patients of 18-45 years age group 39.1% were males and 24.7% females, among 45-60 years age group 22.8% were males and 8.5% females, among > 60years age group all were males.75cases (71.4%) had DF, 27cases (25.7%) DHF and three cases (2.8%) had DSS based on WHO criteria (Figure 2). Two cases (1.9%) died of which one case (0.95%) died of ARDS and other died of MODS (0.95%) .

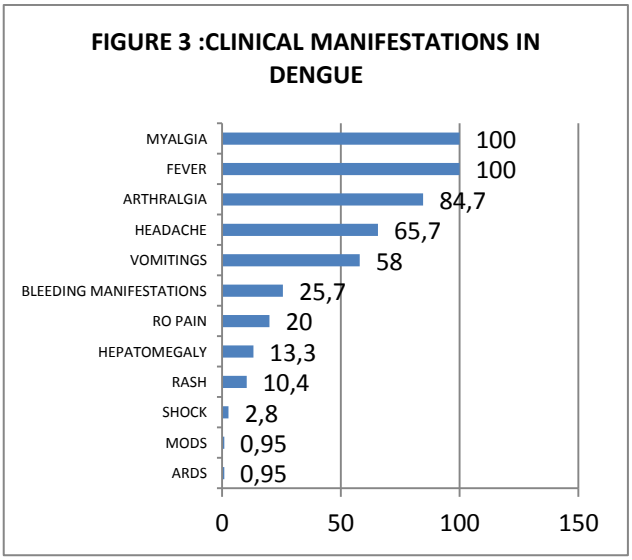
Fever was the most common findings (100%) along with myalgia (100%). Other common symptoms in chronological order included - joint pains (84.7%), headache (65.7%), vomiting (58%), bleeding manifestations (25.7%), retro-orbital pain (20%), rash (10.4%), and shock (2.8 %) (Figure 3) . The clinical spectrum details of DF and DSS are mentioned in Table 1.

Among the bleeding manifestations, melena was the most common seen in 44.4% of DHF patients, followed by skin rash and petechiae (40.7%) , hematuria (18.5%), subconjuctival hemorrhage (11.1%), epistaxis one case (3.7%), gum bleeding (3.7%) and a very rare isolated case of hemoglobinuria (Figure 4). Low platelet count of less than 100,000/cu mm according to WHO criteria was present in 47 (44.7%) patients. Patients having platelet count of < 20000 were five (4.7%), 20000-50000 were nine (8.5%), 50000-100000 were 33(31.4%) and > 1 lakh were 58(55.2%)(Table 4). Thrombocytopenia was seen in 28(37.3%) cases of DF, 16(59.2%) cases of DHF and three (100%) cases of DSS.

Raised serum aminotransferase level (> 2 times upper normal value) was seen in 19 cases(18%) of which 14cases (18.6%) were of DF and five cases (18.5%) were of DHF. Serum CPK levels was elevated in 10 patients (9.5%) of which seven (9.3%) and three patients (11.1%) were of DF and DHF respectively. Serum LDH levels were elevated in nine patients (8.5%) of which six patients (8%) were of DF and three (11.1%) were of DHF. Serological findings are mentioned (Table 3).







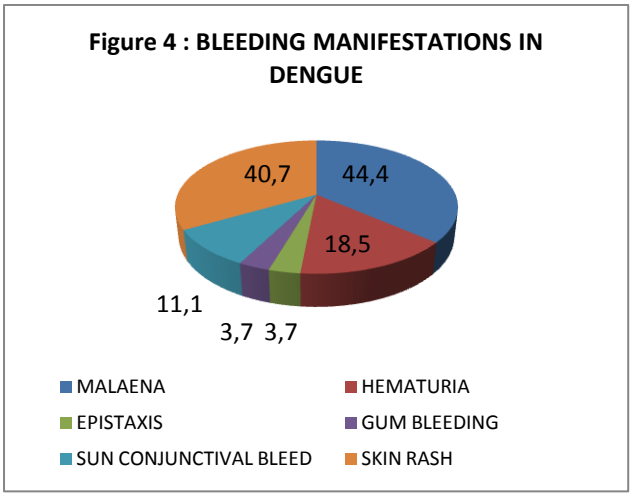


TABLE 1 : Clinical spectrum in dengue

	Total No. (105)(%)	DF (75) (%)	DHF (27) (%)
Number of Males	71(67.6)	50(66.6)	18(66.6)
Number of females	44(32.3)	25(33.3)	9(33.3)
Fever	105(100)	75(100)	27(100)
Myalgia	105(100)	75(100)	27(100)
Headache	69(65.7)	48(64)	21(77.7)
Arthralgia	89(84.7)	66(88)	23(85.1)
Retro-orbital pain	21(20)	13(17.3)	8(29.6)
Vomiting	61(58)	44(58.6)	17(62.9)
Hepatomegaly	14(13.3)	11(14.6)	3(11.1)
Bleeding manifestations	27(25.7)	0	27(100)
Thrombocytopenia	47	28(37.3%)	16(59.2%)

TABLE 2: Lab profile in patients of Dengue

	Total Dengue Positive (n=105)	Dengue Fever (n=75)	DHF (n=27)	P value
Thrombocytopenia	47 (44.7%)	28(37.3%)	16(59.2%)	0.01
CPK	10(9.5%)	7(9.3%)	3(11.1%)	0.20
LDH	9(8.5%)	6(8%)	3(11.1%)	0.37
SGOT (>2 UNL)	19(18%)	14(18.6%)	5(18.5%)	0.382
SGPT (> 2 UNL)	18(17.1%)	13(17.3%)	5(18.5%)	0.491

TABLE 3: Serology in patients of Dengue

Parameters	Number of positive patients	Percentage (%)
NS1 Ag Only	45	42.8
IgMAb Only	7	6.6
IgGAb only	0	0
IgM&IgG	2	1.9
NS1Ag&IgM	29	27.6
Ns1Ag &IgG	5	4.7
Ns1 Ag , IgM&IgG	16	15.2

TABLE 4: Platelet count in Dengue

Platelet count	No. of patients	Percentage (%)
< 20000	5	4.5
20000-50000	9	8.5
50000-100000	33	31.4
>100000	58	55.2

DISCUSSION

The epidemio-clinical profile of dengue has been changing progressively in last few years. In our study, 67.6% cases were males and 32.3% were females. Similar observations were found in the study conducted by Bhaswati Bandyopadhyayet al[5].Male to female ratio in our study was very similar to study of Rashmi KS et al[6] in which , the male-to-female ratio was 1.7:1.Most common clinical manifestation was fever and myalgia (100%) followed by joint pains ,headache (65.7%), vomiting (58%). Analogous findings were observed by Mandal SK et al[7] in their study. Headache was found in 65.7% cases similar to that found by N.P. Singh et al[8] in 2003(61.6%) and 54% by V.K.Singh[9] and others. Retro-orbital pain in our study was found in only 20% cases as contrast to some of the other studies where it was one of the most common presentation.

Hepatomegaly was found in 13.3% cases, similar to that found by N.P.Singh[8] and others. Sharma SK[10] et al found hepatomegaly in 20.4% patients. Mean age of presentation was 38 years, value higher than observed Sharma et al[10] in 1998. Most of the patients were between 18- 45 years of age.

Malena was the most common bleeding manifestations in our study as opposed to skin rash and petechiae in 2008 by Subhash Giri et al[11].Skin rash was present in 40.7% cases of DHF as was reported by Sharma et al and 40% by Aikat BK[12] and others in Kolkata. Low platelet count of less than 100,000/cu mm according to WHO criteria was present in 44.7% patients, lower than that found by N.P.Singh[8] and others. Although severe thrombocytopenia ofless than 10000/cmm was reported in 4.7% patients, lowest recorded being 2000 /mm3 in a DSS case , the overall mortality rate was only 1.9% .Most of the cases admitted with bleeding manifestations did not bleed subsequently

though there was dip in platelet count (some even < 20000/mm3) during hospital study indicating poor correlation between thrombocytopenia and bleeding tendencies, an observation similar to the one made by Sharma et al[10] indicating thereby that the abnormal platelet aggregation rather than reduction in absolute numbers was the cause of bleeding diathesis along with the cytokine mediated endothelial injury. So, in management of DF/DHF immediate replacement of plasma loss by rapid volume expanders is the most important therapy. Thrombocytopenia severity had correlation with severe types of dengue as in Table 2, p value was significant

The levels of AST were equal to or greater than those of ALT levels in all of dengue infected patients, a similar observation by Ritu Karoli et al[1] and Khan AH et al[14] in their study. However the incidence in our study was 18-19% as compared to 86%. Fulminant hepatic failure was reported in one of the studies wherein AST >1000 U/L..In "Nice study" in Brazil by Silva EM et al , cause of hepatic dysfunction was attributed to interaction of C1q and NS1 in liver cells. As per WHO 2009 guidelines, elevation of AST and ALT >1000 U/L was criteria for severe dengue. Although aminotransferase levels increase in conjunction with dengue severity, AST/ALT levels did not discriminate DF and DHF as per study of Lee et al [15],reflecting a similar result in our study (Table 2) .NS 1 Ag only was positive in 42.8% cases, NS 1 Ag, IgM&IgG all three were positive in 16(15.2%) cases. This finding was also observed in study conducted by Rashmi KS et al[6].

Atypical manifestations have been reported in many studies. These include neurological presentation (AIDP, ADEM, encephalopathy, facial palsy), gastrointestinal symptoms (acalculouscholecystitis, fulminant hepatic failure, acute pancreatitis, Gall bladder wall edema), musculoskeletal symptoms (myositis), acute renal failure (rhabdomyolysis), respiratory symptoms (ARDS). In our study atypical cases were reported though less in number. These were – one case of ARDS, one case of haemoglobinuria , ten cases of raised CPK and nine cases of elevated LDH. Cases with higher levels of CPK, LDH and low levels of total serum albumin , total cholesterol, triglycerides are biochemical markers of severity of dengue presentation. In our study, cases of raised CPK and LDH was found (Table 2) but severity with dengue presentation could not be related (p value > .05)

An isolated case of hemoglobinuria, a very rare manifestation of dengue fever was seen. A 26 year male presented with fever and subsequently developed dark coloured urine, was meticulously investigated as per the standard protocol and was found to be seropositive for dengue. No abnormality was detected on urine routine examination, 2-3 RBC/hpf and platelet count was 45000/mm^3, raised serum LDH level (3068), urine dipstick test for hemoglobin was positive and benzidine test was negative. Patient improved after conservative management.

CONCLUSION

In last few years, protean manifestations of the dengue fever was noted in the different parts of the world and more so over in same geographical area and in same time. Apart from typical manifestations, atypical presentations are on rise, which makes the diagnosis an even more challenging and interesting for researchers. Continuous surveillance and timely interventions will minimize the complications, outbreak and mortality.

REFERENCES

1. Dengue in Kerala: A critical review. ICMR Bulletin. 2006;36:13–22.
2. Fever in Chittagong, Bangladesh. ChattMaa Shi Hosp Med Coll J 2013; 12(1): 38–40.
3. Anuradha S, Singh NP, Rizvi SN, Agarwal SK, Gur R, MathurMD.The 1996 outbreak of dengue haemorrhagic fever in Delhi, India;Southeast Asian J Trop Med Public Health: 1998 Sep;29(3):503-6.
4. Sultana N, Biswas SK, Sultan T, Ahmed S, Hossain Z, Chowdhury R. Seroprevalence of

dengue.,CMOS Hospital Medical College Journal,Jan 13,vol 12 issue1

5. BhaswatiBandyopadhyay, Indrani Bhattacharyya, SrimaAdhikary, et al., "A Comprehensive Study on the 2012 Dengue Fever Outbreak in Kolkata, India," ISRN Virology,:2013;vol 2013 Article ID 207580, 5 pages. Available from http://www.hindawi.com/journals/isrn.virology/2013/207580/abs.
6. Rashmi KS, Jagadeesh, Ravikumar KL, PratibhaMalini J, GiridharUpadhyaya P, ArunKaushik R. Serological markers prevalence and trend of probable dengue infection at a tertiary care hospital in Bangalore. Journal of Evolution of Medical and Dental Sciences 2013 September 9 ;2(36); 6968-6976.
7. Mandal SK, Ganguly J, Sil K, Chatterjee S, Chatterjee K, Sarkar P, Hazra S, Sardar D. Clinical Profiles of Dengue Fever in a Teaching Hospital of Eastern India. Natl J Med Res. 2013; 3(2): 173-176.
8. Singh NP, Jhamb R, Agarwal SK, Gaiha M, Dewan R, Daga MK, Chakravarti A, Kumar S.
9. The 2003 outbreak of Dengue fever in Delhi, India.Southeast Asian J Trop Med Public Health. 2005 Sep;36(5):1174-8.
10. VK Singh, JM Haria, SK Jain. "Hospital Based Study of Dengue Hemorrhagic Fever in Western Uttar Pradesh Region". International Journal of Scientifi c Study. 2014;1(5):32-34
11. SHARMA, S. et al. Clinical profile of dengue haemorrhagic fever in adults during 1996: outbreak in Delhi, India. Dengue Bull., New Delhi, v.22, p.20-27, 1998.
12. SubhashGiri, Vishal Sharma, BijoyEasow, Mukul P. Agarwal, Alka Sharma. Low mortality during 2008 outbreak of dengue in Delhi, India: a clinico- biochemical study, Department of Medicine, University College of Medical Sciences (University of Delhi) and GTB Hospital; 2GTB Hospital; Delhi, IndiaR. Ci. méd. biol. 2010; 9(1):10-12.
13. Aikat BK, Konar NR, Banerjee G. Haemorrhagic fever in Calcutta area. Indian J Med Res 1964;52:660-75.
14. RituKaroli, Jalees Fatima, Zeba Siddiqi, Khursheed I. Kazmi, Amit R. Sultania Department of Medicine, Era's Lucknow Medical College,J Infect DevCtries 2012; 6(7):551-554.
15. Khan AH , Hayat AS , Massood N , Solangi , Shaikh TZ.Frequency and clinical presentation at tertiary care hospital of Hyderabad. JLUMHS May-Aug 2010;9(2):88-94
16. Lee et al.Clinical relevance and discriminative value of elevated transaminases for dengue severity .PLOS Ngl Trop dis ;6(6):e1676