Original Article

Comparison of Clinical and Laboratory Profile of Laboratory Positive Dengue and Negative Suspected Dengue cases in a Tertiary Care Hospital, Andhra Pradesh, India

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ABTRACT

Aim: To study the clinical and laboratory profile in laboratory positive dengue and laboratory negative suspected dengue in children in a tertiary care centre.

Materials and Methods: This retrospective study was carried out in a tertiary care hospital at Karimnagar, Andhra Pradesh. 89 cases admitted with fever and thrombocytopenia from June 2012 through December 2012 were considered. Based on the laboratory criteria, they were classified as laboratory positive dengue and laboratory negative dengue.

Results: Of 89 cases admitted with fever and thrombocytopenia, 22 (24.71%) were positive for dengue and 67 cases (75.28%) were negative. The median age of presentation in both the groups was 9 years. Males were more commonly affected in laboratory positive dengue group than dengue negative. Compared with laboratory negative dengue cases, patients with laboratory positive dengue cases were significantly more likely to have rash, pain abdomen and vomiting. There was no statistical significant difference between them in laboratory parameters.

Conclusion: During epidemic of dengue, children presenting with rash, pain abdomen and vomiting are more likely to have dengue fever than children presenting with upper respiratory tract symptoms. As there is no great difference in the laboratory parameters between laboratory positive dengue cases and laboratory negative dengue cases hence children in both the groups may be managed in lines of dengue.

Keywords: Laboratory positive dengue, laboratory negative suspected dengue.

INTRODUCTION

Dengue virus belongs to family Flaviviridae, having four serotypes that spread by the bite of infected Aedes mosquitoes. It causes a wide spectrum of illness from mild asymptomatic illness to severe fatal dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS). Approximately 2.5 billion people live in dengue-risk regions with about 100 million new cases each year[1].In India, the first epidemic of clinical dengue-like illness was recorded in Madras (now Chennai) in 1780 and the first virologically proved epidemic of dengue fever (DF) occurred in Calcutta (now Kolkata) and Eastern Coast of India in 1963-1964 year worldwide[2-4]. Dengue fever and especially dengue hemorrhagic fever ranks highly among the new and newly emerging infectious disease in public health significance and is considered the most important of the arthropod borne viral disease [5].

The 1997 classification divided dengue into

undifferentiated fever, dengue fever (DF), and dengue haemorrhagic fever (DHF). The WHO 2009 classification divides dengue fever into two groups: uncomplicated and severe form. The uncomplicated form includes dengue without warning signs and dengue with warning signs [6].

In tropical countries and possibly elsewhere, dengue fever can be confused with other common tropical infections like leptospirosis, typhus fever, chikungunya, malaria, enteric fever, hantavirus because they present with similar clinical manifestations during the initial phase. A comparison study was done between dengue and dengue like illness by Christopher et al. who has categorized patients with suspecting dengue into laboratory positive dengue and laboratory negative dengue based on the laboratory investigations such as anti-dengue IgM, ELISA and RT-PCR[7] . The present study describes the clinical and laboratory profile of patients with laboratory positive dengue and laboratory negative dengue from a tertiary care hospital.

MATERIALS AND METHODS

This retrospective study was conducted at Chalmeda Anand Rao Institute of Medical Sciences at Karimnagar, Andhra Pradesh from June 2012 through December 2012.Study included children (6 months-14years) admitted with acute febrile illness and thrombocytopenia. For each patient, basic demographics (age,sex), presenting complaints(fever, headache, vomiting, pain abdomen, rash, bleeding manifestations), results of laboratory investigations (hemoglobin, total leucocyte count, haemotocrit and platelet count)at the time of admission and duration of hospitalization were recorded. Hemoglobin(Hb), Total leucocyte count(TLC), hematocrit(PCV) and platelet were done by coulter method(SYSMEX KX21) . Dengue test (NS1Ag, IgG,IgM)were done by rapid diagnostic kits. Other tests included malaria, HIV (rapid diagnostic tests), enteric fever (widal).Cases tested positive for malaria, typhoid, ITP, HIV were excluded. Patients were categorized as Laboratory positive dengue case (LPDC) and Laboratory negative dengue case. Groups of presenting symptoms were analyzed. Dengue fever was further categorized into dengue without warning signs, with warning signs and severe dengue according to WHO classification [6]

Case Definitions

Laboratory Positive Dengue Case [LPDC]

A case of suspected dengue with either NS1Ag or anti-dengue IgM positive, were considered as dengue positive cases.

Laboratory Negative Suspected Dengue Case [LNSDC]

A suspected dengue case that is negative for NS1Ag, anti-dengue IgM antibodies were considered as dengue negative case.

Frequency and 95% confidence interval was calculated for categorical variables, median and inter-quartile range was calculated for non-normally distributed quantitative variables. Mann-Whitney U test was done to see the significant difference between non normally distributed quantitative variables for two groups. Statistical analysis was conducted using Epi info version 7.P value of 0.05 was taken as significant.

RESULTS

A total of 89 childrens with fever and thrombocytopenia were admitted. 22(24.71%) were positive for dengue(10-IgM, 10-NS1Ag, 2-NS1Ag and IgM positive)and were categorized as laboratory positive dengue, the remaining 67(75.28%) were categorized as laboratory negative dengue cases.11 cases(50%) were dengue without warning signs, 10 cases(45.45%) were dengue with warning signs and one severe dengue case(4.54%) .The median age of children in both the categories was 9 years (median 5-11yrs). Patients with laboratory positive dengue were more likely to be males than those who were laboratory negative(68% and 52% respectively).On the other hand females were more in LNSDC than LPDC(47% and 31% respectively).They were few differences in frequency of presenting symptoms between patients with laboratory positive dengue and patients that were dengue-laboratory negative(Table 1).Compared with laboratory dengue negative patients, patients with laboratory positive dengue infections were significantly more likely to have rash, pain abdomen and vomiting. In contrast patients with laboratory positive dengue infections were significantly less likely than laboratory negative patients to have symptoms of upper respiratory tract infection such as cold and cough and also less likely to have convulsions. There was no significant difference between groups in the proportion of patients with bleeding manifestations and combination of headache and vomiting.

There was no statistical significant difference between medians of laboratory positive dengue cases and laboratory negative dengue cases in laboratory parameters such as hemoglobin(Hb), total leucocyte count(TLC), neutrophils, lymphocytes, monocytes, eosinophils, basophils, packed cell volume(PCV), platelet count at the time of admission and lowest platelet count during hospital stay. The average stay in hospital in both the categories were 5 days [Table 2]. 81(91.01%) cases got cured, 7 cases (7.87%) left against medical advice (LAMA) and one case expired which was a case of severe dengue.

Table1: Frequency of presenting symptoms between LPDC AND LNSDC

VARIABLES	LAB POSITIVE DENGUE % (number) CI [lower-upper]	LAB NEGATIVE DENGUE % (number) CI [lower-upper]
Sex: Males	68.18 (15) [45.13-86.14]	52.24 (35) [39.67-64.60]
Females	31.82 (7) [13.86-54.87]	47.76 (32) [35.40-60.33]
Fever, Bleeding Manifestations	4.559 (1) [0.12-22.84]	4.48 (3) [0.93-12.53]
Fever, Headache, Vomiting	4.55 (1) [0.12-22.84]	4.48 (3) [0.93-12.53]
Fever,Cough,Cold	13.64 (3)[2.91-34.91]	32.84 (22) [21.85-45.40]
Fever, Pain Abdomen	13.64 (3) [2.91-34.91]	4.48 (3) [0.93-12.53]
Fever, Rashs	9.09 (2) [1.12-29.16]	1.49 (1) [0.04-8.04]
Fever, Vomitting	22.73 (5) [7.82-45.37]	17.91 (12) [9.61-29.20]
Fever, Seizure	0.00 (0) [0.00-15.44]	2.99 (2) [0.36-10.37]

Table 2: Differences between laboratory parameters of LPDC and LNSDC with P value.

	Laboratory Positive Dengue Cases[LPDC]	Laboratory Negative Dengue Cases[LNSDC]	
Variables	Median(Iqr)	Median(Iqr)	P Value
Age (Years)	9.5[5-11]	9[4-12]	0.72
PCV (%)	31.5[29.4-38.0]	32[28-35.5]	0.50
Platelets at Admission (Per Cu.Mm)	0.64[0.3-0.8]	0.73[0.4-1.03]	0.24
Lowest Platelet Count (Per Cu.Mm)	0.54[0.20-0.76]	0.58[0.40-0.90]	0.19
Hb(Gm/Dl)	10.75[9.8-12.5]	10.8[9.4-12]	0.56
TLC(Cells/Cu.Mm)	4100[3200-6500]	4500[3000-6000]	0.81
Neutrophils (%)	50[21-57]	45[33-60]	0.54
Lymphocytes (%)	43[33-54]	46[34-57]	0.49
Monocytes (%)	4[3-5]	3[2-6]	0.39
Eosinophils (%)	3[2-5]	3[2-4]	0.3
Basophils (%)	0[0-0]	0[0-0]	0.41
Stay In Hospital (Days)	6[4-7]	5[4-6]	0.54

DISCUSSION

Dengue is the world's most common mosquito-borne viral infection and a leading cause of morbidity throughout the tropics and subtropics [8]. The diagnosis of dengue infection early in the course of illness, before development of severe manifestations of the disease, can be challenging. Serologic tests, the mainstay of laboratory diagnosis, are unreliable early in infection (during first 3 days after symptoms onset) and usually require collection of paired acute and convalescent phase samples. Polymerase chain reaction (PCR) testing, which is more sensitive early in dengue infection, is usually unavailable in the countries with the highest burden of disease. Therefore diagnosis of dengue fever relies on recognition of clinical features along with serological confirmation. In our study single anti dengue-IgM and NS1Ag were considered positive and there was no significant difference in the laboratory parameters between two groups but there was significant difference in clinical presentation.

In our study the median age of presentation in both the groups was 9 years, whereas according to Christopher et al. patients with LPDC were older (median 18 years) than patients who were laboratory negative for dengue infection. In the same study patients with laboratory positive dengue infections were more likely to be males than those who were laboratory negative for dengue, which was a similar finding in our study [7].

According to the new WHO dengue case definition, rash, pain abdomen, vomitings are some of the symptoms included in the new guidelines [6]. In our study laboratory positive dengue cases were significantly more likely to have rash, pain abdomen, vomitings and less likely to have upper respiratory tract symptom. A similar study done by Christopher et al. shows that laboratory positive dengue infections were significantly more likely to have retro-orbital pain, rash, joint pain and body aches and less likely to have upper respiratory tract infections, which is a similar finding in our study[7].The presence of rash in dengue positive cases is also a significant finding in certain studies done in adults [9,10,11,12] and absence of upper respiratory symptoms in dengue positive cases is also a significant finding in previous studies done in children [13,14]. Four studies, which included patients of all age groups have found that frequency of rash was higher in patients with dengue (Deparis et al.1998; Nunes-Araujo et al.2003; Hammond et al.2005)[15,16,9], this finding is consistent with our study done in children only. In contrary to our study, two studies which assessed children only found no significant association with rash(Sawasdivorn et al. 2001; Karande et al. 2005)[17,18] . According to Kalayanarooj S et al. children with dengue were more likely than children with other febrile illnesses (OFI) to report anorexia, nausea and vomiting [19] which is in similar to our study, where vomiting are more common in dengue positive cases than dengue negative cases.

In the present study, there was no significant difference between groups in the proportion of patients with bleeding manifestations and headache, similar to a study done by Nunes-Araujo et al . who reported that fever,

headache, myalgia, retro orbital pain and arthralgia were the most commonly reported symptoms among confirmed dengue cases whereas hemorrhagic manifestations were uncommon[16]. These findings are supported by three more studies (Deparis et al.1998; Hammond et al.2005; Phuong et al.2006) where frequency of hemorrhagic signs showed no differences between dengue and other febrile illnesses[15,9,13].

Neutrophil and lymphocyte counts were significantly lower in dengue patients than in OFI patients among studies that measured these variables (Kalayanarooj et al. 1997; Deparis et al. 1998; Phuong et al.2004; Wilder-Smith et al.2004; Hammond et al. 2005; Karande et al.2005; Chadwick et al.2006; Low et al. 2006)[19,15,13,12, 9,18,10,20] which is in contrary to our study, but for one retrospective study by Sawasdivorn et al.(2001) which showed no association between these variables in laboratory dengue positive cases and laboratory dengue negative cases[17] . In the present study there has been no significant difference in the haemotocrit values between LPDC and LNDC, this finding is further supported by Deporis et al; Buchy et al; Kalayanarooj S et al; Low et al [15,21,19,20]. Leucopenia is one of the manifestations of dengue listed in the current WHO case definition but it is a common clinical finding in many viral childhood infections [22] and as children have an average of 6 to 8 viral infections annually [23,24] the finding that this is not a good early predictor for dengue among children could be anticipated. Although a previous study from Thailand did identify leucopenia as a good early predictor of dengue infection in children [21]. Another study from Nicaragua found that leucopenia was significantly associated with early dengue infection in adults but not in children [9], these findings are similar to the present study where leucopenia is not significantly associated with dengue infection in children. The average duration of hospital stay in both the categories were same.

A recent systematic review identified that among the 49 studies reviewed, 18 studies lacked statistical comparison in clinical and laboratory profile between dengue and OFI, similar to our study which found no significant difference between laboratory positive dengue and laboratory negative dengue in laboratory parameters. In 15 studies that have been examined there were differences in clinical and laboratory features between dengue and other febrile illnesses [25].

Nonetheless, the study has several limitations. Because of the retrospective nature of our study, we were unable to assess certain variables and also unable to assess the variation in clinical and laboratory features predictive of dengue by day of illness. Due to less availability of resources confirmatory test for dengue i.e ELISA, RT-PCR and other tests to diagnose leptospirosis, typhus group and other viral infections was not done which might have been included in laboratory negative dengue cases.

CONCLUSION

During epidemic of dengue children presenting with rash, pain abdomen and vomiting are more likely to have dengue infection than children presenting with upper respiratory tract symptoms. As there is no great difference in the laboratory parameters between laboratory positive dengue and laboratory negative dengue cases, children in both the groups can be managed in lines of dengue.

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