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HAEMATOLOGICAL CHANGES IN DENGUE FEVER

Shaista Choudhary[1],B.R Shivkumar[2], Adisesha Shankar[3], Y.A. Manjunatha[4], M.M. Priyadarshini[5]

ABSTRACT

Dengue infection has been known in India for a very long time. Frequent epidemic episodes occur especially in monsoons. All ages and both sexes are susceptible to dengue fever. Dengue/D.H.F (dengue hemorrhagic fever) is widely prevalent in our country. All four serotypes have been reported. It is one disease where worst outcome can be prevented by early diagnosis. It has been classified into three broad categories for management purpose and the classification is based upon clinical features and laboratory parameters.

Group A -patients with uncomplicated disease who need not be admitted.

(Stable haematocrit but decreasing white blood cell count)

Group B -Patients for in hospital management.

(Increase in haematocrit, decrease in w.b.c count and platelets)

Group C -Patients who require emergency treatment and urgent referral.

(Rapidly falling platelet count, altered liver function tests, renal function tests and increasing haematocrit)

Hence laboratory tests play a centre role in early diagnosis of dengue fever and its complications. In our study we have emphasized upon the haematological parameters clinical signs and symptoms and its correlation with dengue infection.

Keywords: dengue fever, haematological parameters, atypical lymphocytes.

INTRODUCTION

Dengue infection is the most rapidly spreading mosquito borne viral disease in the world.[1]Dengue viruses (DEN V) are classified into four serotypes-DEN V-1,2,3 &4).In humans DEN V infection leads to a spectrum of clinical manifestations that range from in apparent or mild febrile illness as dengue fever(DF) to its complications such as dengue haemorrhagic fever(DHF) and dengue shock syndrome (DSS).[2]Dengue fever is a self limiting disease and represents majority of cases of dengue infection. A prevalence of Aedes aegypti and aedes albopictus together with the circulation of dengue virus of more than one type in any particular area tends to be associated with outbreaks of DHF/DSS. [3]Classical dengue or break-bone fever has been known in India for a very long time. It is an acute viral infection caused by at least 4 serotypes of dengue virus. [3]

In India dengue virus was first isolated in 1946 and major outbreaks have been reported since then. Dengue hemorrhagic fever was first reported in Calcutta in 1963.[4] Dengue fever can occur endemically as well as epidemically. Epidemics can be explosive and often start during monsoon when breeding of vector mosquitoes is abundant. Temperature also plays an important role. Mosquitoes kept at 26 degree Celsius fail to transmit DEN-2 virus. Hence the low incidence of DHF in certain seasons could be explained by this observation.[3, 5]

SCENARIO IN INDIA: Dengue infection is one of the leading cause of death and hospitalization in India. According to world health organization, dengue infection has existed in India for more than a century. Few studies have examined the cause of the disease and its impact on the general population still there is a need to discover the tools for early diagnosis [6] Dengue infection from being a sporadic illness has become a regular post monsoon feature in many regions. [7]

MATERIALS AND METHODS

The material comprised of 210 cases of dengue infection admitted to medicine department of our hospital from

[1]Associate Professor, Department of Pathology, B.R.Ambedkar Medical College, Bangalore.
[2]Professor Dept of Medicine, B.R. Ambedkar Medical College,
[3]Professor & HOD, Department of Pathology, Annapurna Medical College, Peeriaseegapadi, Salem.
[4]Professor & HOD, Department of Pathology, B.R.Ambedkar Medical College, Bangalore.
[5]Post graduate in Pathology, B.R.Ambedkar Medical College, Bangalore.

July2009 to May 2011, with clinical history suggestive of dengue infection. Out of these 210 cases, patients with positive serology for dengue infection were studied in detail to evaluate the haematological changes. Case definition was based on W.H.O criteria and confirmed by positive serology to dengue fever. Performa was prepared which included clinical details and information on various parameters of blood count, coagulation profile and biochemical tests. Details of chest X-ray and other imaging modalities were also recorded wherever required. Serum from all clinically suspected cases was tested in central laboratory of our hospital for anti-dengue immunoglobulin (IgG &IgM) by solid phase enzyme immunoassay based on immunocapture principal. Cases positive for dengue infection were followed for clinical and laboratory profile including peripheral smears for atypical lymphocytes.

RESULTS

During the study period 210 cases were admitted with suspected dengue infection. Out of these 96 patients were confirmed by serology (ELISA method) to be dengue infection positive.

Age range was from 18years to 57 years. There was variation in frequency of cases in different months. Maximum numbers of cases were seen during late summer and entire rainy season i.e. June to September.The clinical features included fever, headache, vomiting, myalgia, body rash and mucosal bleeding.Table-1 shows the summary of clinical features. Amongst the haematological features, most common abnormality was thrombocytopenia(83%) followed by leucopoenia(79%)and raised S.G.O.T and

S.G.P.T.The findings are illustrated in table-2.Two patients had features of dengue hemorrhagic fever and one had features of dengue shock syndrome. Raised hematocrit was found in 12 patients.Thromboplastin time was significantly raised in 20 patients, increased creatine kinase levels were seen in 5 patients. Peripheral smear examination showed atypical lymphocytes in 18 patients, the characteristic findings were plasmacytoid lymphocytes, slicing of nucleus and irregular nuclear border.

TABLE 1: Clinical manifestations of patients with dengue infection

Feature	No . of cases (%)
Fever	95(99)
V omiting	70(73)
H eadache	78(81)
M yalgias	75(78)
Diarrhea	10(10)
R ash	4(4)
Gingival bleeding	2(2)
Positive tourniquet test	2(2)
H epatomegaly	34(35)
S plenomegaly	5(5)
Pleural effusion	1(1)

TABLE 2: Profile of abnormal laboratory investigations in patients with dengue infection

Investigations	No. of cases (%)
Platelet count (per mm^3)	80(83)
>100000	10(10)
50000-100000	12(12.5)
<50000	58(60)
White blood cell count (per mm^3)	76(79)
Liver function test	
Serum bilirubin(>1mg/dl)	35(36)
Serum aspartate transaminase >40IU/L	62(64)
Serum Alanine transaminase >40IU/L	62(64)
Partial thromboplastin time	20(20)
>2 fold(PTT) versus controls	
Creatine kinase(175 IU/L)	5(5)
Atypical lymphocytes	18(18)

Figure 1- Atypical lymphocytes showing nuclear slicing H&E X400

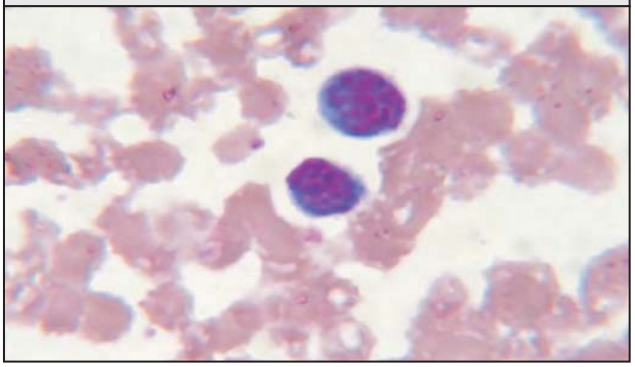


Figure 2-Coparison of a normal lymphocyte with a reactive lymphocyte H&EX400

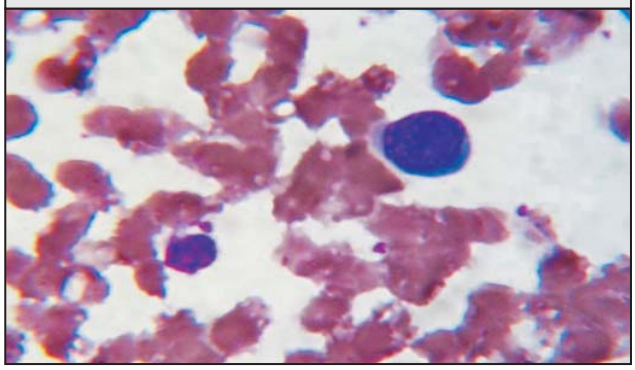


Figure 3-Comparison of a normal lymphocyte with an enlarged reactive lymphocyte H&E X400

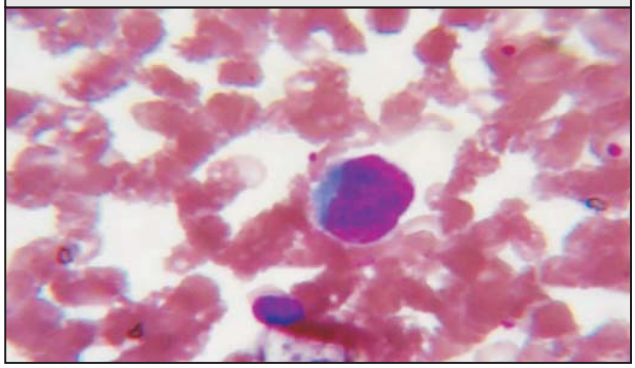


Figure 4-A lymphocyte showing lobed nucleus H&E X400

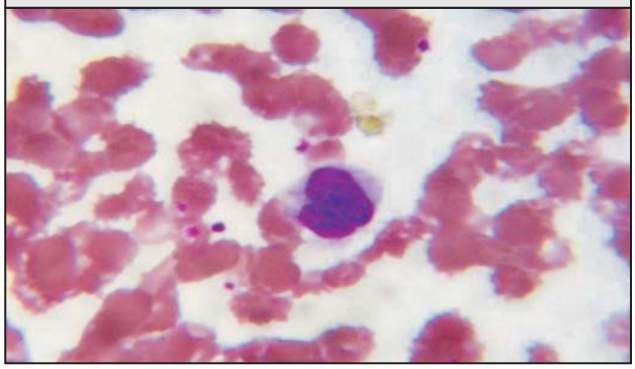
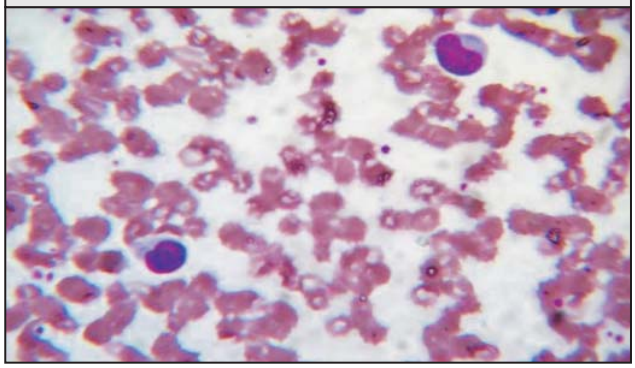


Figure5-A plasmacytoid lymphocyte H&E X400



DISCUSSION

Dengue viral infection has been known in India for over two centuries. Certain areas show endemicity for the virus whereas others have reported epidemics.

Dengue viruses belonging to the genus Flaviviridae has antigenically four distinct serotypes DEN-1 to DEN-4.Dengue virus causes a broad spectrum of illness ranging from mild fever to classical dengue hemorrhagic fever and shock syndrome. Each serotype of virus produces lifelong immunity but provides only short term cross immunity. It is thought that the homologous antibodies from previous infections act as non-neutralizing antibodies in any subsequent infection with a different serotype of the virus and forms new complexes with new infecting serotypes. These complexes can cause the antibody dependent enhancement of heterotypic secondary dengue infection. [9]The present strategy is to control infection and prevent complications. For the prevention and control of dengue infection W.H.O has proposed bioregional dengue strategy for south-east Asia and Western Pacific region. It consists of six elements, research being one of the elements. [10]

In the present study emphasis was laid upon haematological investigations of patients along with clinical features. Out of 96 cases studied 2 cases turned out to be dengue hemorrhagic fever and one case of shock syndrome. Clinical features are illustrated in table-1.

All the patients had fever on presentation. Besides fever, headache myalgia and vomiting were other common clinical features. Studies done earlier also show similar presentation.[11,13,15]Two patients presented with body rash and gingival bleeding and epistaxis. They were categorised in D.H.F according to W.H.O criteria, though previous studies have reported a higher incidence of hemorrhagic manifestations.[11]

Most significant laboratory abnormality in present study was thrombocytopenia(83%).Table -2 shows the haematological parameters.It may be attributed to

depression of bone marrow due to acute stage of viral infection.[9]Incidence of leucopoenia was 31% in a study by Jain P.K. et.al.The incidence of bleeding as reported by Chandrakanta et.al. (2008) was 38.8% out of which 23.7% cases had gastrointestinal tract bleeding. Jain P.K et.al reported bleeding in 32% cases. In our study2% of cases had gingival bleeding. Ayub et.al.(2006) have reported gingival and gastrointestinal tract bleeding in 10% of cases.[12]Jonathan G Lim studied the profile of paediatric patients with D.F and D.H.F.Though mild bleeding was seen but shock was uncommon in their study.[13]

Liver function tests showed significant alteration in their values suggesting liver damage. It could be attributed to the viral protein NS-1, since it occurs in the liver. The amount of NS-1 accumulated would depend upon the virulence of each particular strain and serotype infecting the liver cells. It is therefore important to assess the clinical and laboratory differences between DF and DHF during admission to health centres. [2]In a study by Irfan Arshad et.al it was concluded that haematological parameters like prolonged APTT and raised hematocrit and biochemical parameters have strong association with the complications of dengue fever and hence are associated with poor outcome of disease.[5]In the present study partial thromboplastin time (PTT) was raised two folds in 20% cases. Irfan Arshad has reported prolonged APTT in 26% cases, whereas Ayub et.al has reported 10% in their studies. [5, 9]Ali Netal (2007) have found 26.6% leucopenia and 77.1% thrombocytopenia at the time of admission. 2.5% and 16.7% patients had deranged P.T and APTT. Atypical lymphocytes were seen seen in 52% of smears. [14]Vinod H.Ratageri have reported neurological involvement in their study. Neurological manifestations range from non specific symptoms to encephalitis and rarely Gullien Barre syndrome.[15]

We studied the peripheral smear of all the patients. Figures 1-5 depicts the reactive changes in lymphocytes.18% of smears showed reactive lymphocytosis with atypical lymphocytes. These included plasmacytoid type of lymphocytes with nucleus pushed to periphery, slicing of nucleus, irregular border of nucleus, bilobed nucleus. Few authors have studied the smears and reported similar findings. Thisyakorn et.al. (1984) have reported atypical lymphocytes in majority of cases of dengue hemorrhagic fever whereas Gawoski J M et.al. (2003) have reported 9% abnormal plasmacytoid lymphocytes.[16.17]

CONCLUSION

As dengue infection is increasing in incidence we need to have improved diagnostic modalities. Early detection of severe cases and efficient medical management are of prime importance in all areas where it is endemic.[18]One must correlate the clinical feature, laboratory parameters including the peripheral smear examination so that early diagnosis and management can be done and one can avoid complications. It is mandatory for a haematologist to screen the smears for atypical lymphocytes while doing platelet count.

This would definitely help when it comes to early diagnosis and prompt treatment.

REFERENCES

1. Ragini Mishra, Prashanth Kumar. A study on outbreak of dengue from Bihar, India-establishing new foci, attributable to climatic changes.jour of public health and epidemiology.2011; 3:499-502.
2. M.Vazquez-Pichardo,C.Rosales-jimenez,O.Rojas-Espinosa,I.Lopez-Martinez and M.M.B.Moreno-Altamirano. Is liver damage dependent on the serotype of dengue virus?-A study in Mexico.2006;30:114-120.
3. K. Park. Arthropod borne infections In :Park's Textbook of Preventive and Social Medicine.21st edition;224-225.
4. Arindam Sarkar, Debjani Taraphdar, and Shyamalendu Chatterjee.Molecular typing of dengue virus circulating in Kolkata. India. jour of tropical medicine.2012;1-5.
5. Irfan Arshad, Aamir Hussain,Fayyaz Ahmed Malik,Shahida A.R.Shah.Clinico-pathologic correlations and their associations with poor outcome. Professional med J. 2011;18(1):57-63.
6. Amit T. Bhavsar, Donald S.Shepard, Jose A. Suaya, Moses Mafowosofo,Clare I. Hurley and Marion W.Howard.A private hospital-based study assessing knowledge, attitudes, practices and costs associated with dengue illness in Surat, India. Dengue Bulletin 2010; 34:54-63.

7. Ira Shah and Bhushan Katira.Clinical and laboratory abnormalities due to Dengue in hospitalized children in Mumbai in 2004.Dengue bulletin 2005; 29:90-95.
8. M.Kurukumbi, JP Wali, Shobha Broor, P Aggarwal, P Seth , Rohini Handa e.t.al.Seroepidemiology and active surveillance of dengue fever/dengue haemorrhagic fever in Delhi. Indian J of Med Sciences.2001; 55(3):149-156.
9. Muhammad Ayub, Adel M Khazinder,Eman H Lubbad,Shahid Barlas,Adnaan Y Alfi,Sawsan AI-Ukayli.Characteristics of Dengue fever in a large public hospital,Jeddah,Saudi Arabia. J Ayub Med Coll Abbottabad 2006; 18(2).
10. Michael B Nathan, Renu Dayal, Maria Guzman. Dengue in the WHO South-East Asia Region. Dengue guidelines for diagnosis, treatment, prevention and control.2009.
11. Anju Agarwal, Jagdish Chandra, S.Aneja, A.K.Patwari and A.K.Dutta.An epidemic of dengue fever and dengue shock syndrome in children in Delhi. Indian Pediatrics 1998; 35:727-732.
12. Jain P.K, Sharma Awadhesh Kumar, Agarwal Navneet, Siddiqui Mohd Zaki, Pawal Praveen, Gaba Ripudaman et.al. Jour of infectious diseases and immunity 2011;3(7):124-133.
13. Jonathan G.Lim, Salvacion R. Gatchalian, Ma.Rosario Z.Capeding. PIDSP Journal 2010; 11:26-34.
14. Ali N, Usman M, Syed N Khurshid M.Haemorrhagic manifestations and utility of haematological parameters in dengue fever tertiary care centre experience at Karachi. Scand J Infect Dis 2007; 39:1025-8.
15. Vinod H. Ratageri, T.A.Shepur, P.K.Wari,S.C.Chavan,I.B.Mujahid and P.N.Yergolkar.Clinical profile and outcome of dengue fever cases. Indian jour of paediatrics 2005; 72:705-6.
16. Thisyakom U, Nimmannitya S ,Ningsanond V,Soogarun S. Atypical lymphocyte in dengue hemorrhagic fever: its value in diagnosis. Southeast Asian J Trop Med Public Health 1984; 15(1):32-6.
17. Gawoski J M, Ooi W W. Dengue fever mimicking plasma cell leukemia. Arch Pathol Lab Med 2003; 127(8):1026-7.
18. Philip Buchy, Sutee Yosan, Rosanna W, Elizabeth Hunsperger. Laboratory tests for the diagnosis of dengue virus infection. Scientific working group, report on dengue. copyright World health organization research and training in Tropical diseases, 2007.