Evaluation of Hematological and Biochemical Profile of Early Dengue Patients

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ABSTRACT

Introduction: Dengue infection has been identified as the fastest spreading mosquito-borne viral disease by World Health Organization. This study is an attempt to elucidate the positive laboratory profile of serologically diagnosed early dengue patients so as to facilitate early diagnosis, treatment and management.

Material and methods: A total of 100 cases diagnosed as dengue based on rapid immunological card tests (NS1 antigen and Ig M antibodies) were analyzed for haematological and biochemical parameters. Haematological parameters included haemoglobin, hematocrit, TLC, DLC, platelets count and peripheral blood smear. Biochemical parameters including serum Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Total Bilirubin (T. Bil.) and Alkaline phosphatase (ALP).

Result: Haemoglobin ranged from 6.4-17.0 gm/dl. Hematocrit was raised in 06 (06%) cases. Thrombocytopenia (Platelets count <1lakh/mm^3) was seen in 54 (54%) cases. TLC <4,000/mm^3 was seen in 43 (43%) cases and >11,000/mm^3 was seen in 09 (09%) cases. Lymphocytosis and neutrophilia were seen in 40 (40%) and 14 (14%) cases respectively. On peripheral blood smear reactive and plasmacytoid lymphocytes seen. AST, ALT, ALP and Bilirubin were deranged in 64 (64%), 60(60%), 12(12%) and 02(02%) cases respectively.

Conclusion: Haemoconcentration, leucopenia, thrombocytopenia, lymphocytosis, and raised liver enzymes SGOT and SGPT along with reactive/ plasmacytoid lymphocytes on peripheral smear gives enough clues to test for dengue serology so that dengue cases can be diagnosed in their initial stages and prompt management can be started to prevent complications of dengue fever.

Keywords: Dengue, Fever, Leucopenia, Thrombocytopenia, Hematocrit

INTRODUCTION

Dengue fever outbreaks are increasing in India and has established its roots. One state after the other are getting affected. The disease is caused by dengue virus which gets transmitted to humans by the bites of infected mosquitoes *Aedes aegypti* and *Aedes albopictus*. Dengue virus belongs to the genus *Flavivirus* in the family Flaviviridae. There are four antigenetically related but distinct serotypes of the dengue virus: DENV-1, DENV-2, DENV-3, and DENV-4. It is a positive-stranded encapsulated ribonucleic acid (RNA) virus. In humans, one serotype produces lifelong immunity against reinfection but only temporary and partial immunity against the other serotypes[1]. Classic dengue fever is marked by rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation, and a centrifugal maculopapular rash[2]. The WHO 2009 classification divides dengue fever into two groups: Dengue with or without warning signs and severe dengue, though the 1997 WHO classification is still widely used.The 1997 classification divided dengue into 1) Undifferentiated fever 2) Dengue fever (DF) and 3) Dengue haemorrhagic fever (DHF). DHF is further divided in to I to IV Grades. III and IV Grades are called as Dengue Shock Syndrome(DSS)[3,4]. Four main characteristic manifestations of dengue illness are (i) continuous high fever lasting 2-7days (ii) haemorrhagic tendency as shown by a positive tourniquet test, petechiae or epistaxis (iii) thrombocytopoenia (platelet count $<100\times10^9$/l); and (iv) evidence of plasma leakage manifested by haemoconcentration (an increase in haematocrit 20% above average for age, sex and population), pleural effusion and ascites, *etc*.[3,4]. Laboratory diagnosis of dengue is routinely done by demonstration of anti dengue immunoglobulin M (IgM) antibodies or by nonstructural protein 1(NS-1) antigen in patients' serum/plasma depending upon the day of illness using either enzyme-linked immunosorbent assay (ELISA) or immune chromatographic-based rapid card tests. Leukopenia is the most prominent hematological change, sometimes with counts of less than 2.0 x 10^3/µL. However, there are reports of mild leukocytosis at the onset of the disease, with neutrophilia. Lymphocytosis is a common finding, with the presence of atypical lymphocytes. The hematocrit concentration should be monitored according to the days of illness, remembering that, with the progression to DHF, there will be a 20% increase in hematocrit from the patient's baseline, associated with thrombocytopenia (< 100 x 10^9/L)[5,6]. The platelets count tend to fall over course of illness and have been found to predict the severity of the disease[7]. Of biochemical variables, the most frequent changes occur in liver function tests such as in serum aspartate aminotransferase (AST), alanine aminotransferase (ALT),

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Gamma glutamyl transpeptidase, alkaline phosphatase (ALP) and serum albumin concentrations[8]. Clinical diagnosis of early dengue patients is challenging as it presents with nonspecific symptoms, including fever, headache and myalgia. Since there are many infectious diseases which have similar clinical features, a combination of clinical and laboratory parameters in any acute febrile illness could be used as markers to diagnose early dengue infection. So this study is an attempt to elucidate the positive laboratory profile of serologically diagnosed dengue patients so as to facilitates early diagnosis, treatment, management and vector control measures, to reduce the morbidity and mortality because of this disease.

MATERIAL AND METHODS

This study was conducted at PGIMER Satellite Centre, Sangrur. Cases were taken during the dengue outbreak from October 2017 to December 2017. Total 100 cases were taken which were seropositive (Dengue NS1 antigen and IgG and IgM antibodies) using rapid visual card tests (SDQ Dengue Ag + Ab Duo Test) from SD Biosensor healthcare Pvt. Ltd. having sensitivity and specificity of 97.2% and 96.2% respectively. Cases were confirmed at civil hospital, Sangrur by IgM antibody capture ELISA (IgM Mac ELISA) test wherever possible. Dengue seropositive patients brief clinical history along with haematological and biochemical investigations were filled in the proforma after taking proper consent from the patients.

Inclusion Criteria

- Febrile patients with positive NS1 antigen or IgM or both on rapid card tests. IgG may be positive or negative.

Exclusion Criteria

- Patients with only IgG positive on rapid card tests were excluded from the study.
- Patients with other identified illnesses like typhoid, malaria which were coexisted with dengue positive serology were excluded from the study.

Hemogram was done on automated cell counter analyzer (Sysmex XP 100) which included haemoglobin, hematocrit, Total leucocyte count (TLC), Differential leucocyte count (DLC) and platelets count.

Leishman stained Peripheral smears were made of every patient to confirm the automated analyzer values as well as to see the morphology of white blood cells like atypical / reactive/ plasmacytoid lymphocytes. Platelets counts were cross checked on stained smears. Hematocrit raised >20% of normal was considered as hemoconcentration. Leukopenia was taken as total leucocyte count < 4,000 /mm^3. Thrombocytopenia was taken as platelets count < 1,00,000 /mm^3.

Biochemical parameters included serum Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Total Bilirubin (T. Bil.) and Alkaline phosphatase (ALP) were done on cobas c 311 from Roche (Hitachi) biochemistry machine.

Information about patients obtained from proformas were taken in tabulated form in excel sheet and findings were compared with similar studies.

Age (in years)	Male	Female	Total	Percentage (%)
0-10	01	03	04	04
11-20	06	04	10	10
21-30	17	10	27	27
31-40	11	14	25	25
41-50	08	04	12	12
51-60	06	06	12	12
61-70	06	04	10	10
Total	55	45	100	100

Table-1: Distribution of patients according to age and sex (n= 100)

Clinical signs and symptoms	Number of cases	Percentage (%)
Fever	60	60
Fever with associated chills	40	40
Bodyache	85	85
Headache	65	65
Rashes	10	10
Nausea/ Vomiting	20	20
Diarrhoea	05	05
Haemoptysis	02	02
Melaena	02	02
Epistaxis	00	00
Itching	01	01

Table-2: Clinical presentation of patients with dengue fever (n=100)

RESULTS

A total of 100 patients were studied, diagnosed as dengue based on rapid card tests. ELISA (Mac ELISA for IgM) was done in 52 cases out of which dengue positivity was seen in 49 cases. According to WHO criteria 96% patients fall under Dengue Fever (DF), 03% under Dengue Haemorrhagic Fever (DHF) and 01% under Dengue Shock Syndrome (DSS). Haematological and biochemical parameters were done on all 100 patients. Out of 100 cases 55 (55%) were males and 45 (45%) were females. Maximum patients 52 (52%) were in age group of 21-40 years [Table 1]. Fever was present in all patients.The most frequent other symptoms were bodyache 85 (85%), and headache 65(65%) [Table 2]. Haemoglobin ranged from 6.4-17.0 gm/dl and mean haemoglobin was 10.9 gm/dl. Total leucocyte count (TLC) ranged from 1,500-14,400/mm^3 and mean TLC was 4,900/

	<4,000 (mm^3)		4,000-11,000 (mm^3)		>11,000 (mm^3)	
	Male	Female	Male	Female	Male	Female
No.of patients	22	21	30	18	05	04
Percentage	43		48		09	

Table-3: Total Leucocyte Count (TLC) of patients with dengue fever (n=100)

Platelet Count (mm^3)	Male	Female	Total	Percentage (%)
<20,000	01	01	02	02
20,000-50,000	10	04	14	14
50,000- 1lakh	23	15	38	38
1lakh- 1.5 lakhs	12	10	22	22
>1.5 lakhs	10	14	24	24

Table-4: Platelet Count (PC) of patients with dengue fever (n=100)

Parameter		Range	Mean	Remarks
Hemoglobin (gm/dl)		6.4-17.0	10.9	<7 n=2 >7 n=98
Hematocrit (%)		22-55.3	39.97	WNL n=94 >20% of normal n=06
Leucocyte count(mm^3)		1.5-14.4	4.9	<4.0 n= 43 >4.0 n=57
DLC (%)	Neutrophils	15-78	54.18	<72 n=86 >72 n=14
	Lymphocytes	08-80	36.3	<45 n=60 >45 n=40
Platelets count (mm^3)		08,000-2.6 lakhs	95,680	<1.5 lakh n=76 >1.5 lakh n=24

Table-5: Summary of haematological findings in dengue patients

Biochemical test	Range	Mean	Remarks
AST (U/Lt)	22-544	283	< 40 n=36 >40 n=64
ALT (U/Lt)	16-254	135	<40 n=40 >40 n=60
Bilirubin (mg/dl)	0.2-1.5	0.85	< 1.2 n=98 >1.2 n=02
ALP (U/Lt)	41-262	151.5	< 129 n=88 >129 n=12

Table-6: Biochemical findings in Dengue fever (n=100)

mm^3 [Table 3]. Platelets count ranged from 0.8-2.6 lakh/mm^3 and mean platelet count was 95,680/mm^3 [Table 4]. Hematocrit ranged from 22% - 55.3% and mean hematocrit was 39.97%. Lymphocytosis was present in 40 (40%) cases while neutrophilia was seen in 14 (14%) cases [Table 5]. On peripheral blood smear reactive and plasmacytoid lymphocytes seen. AST, ALT, ALP and Bilirubin were deranged in 64 (64%), 60(60%),12(12%) and 02(02%) cases respectively [Table 6].

DISCUSSION

Dengue is haemorrhagic viral fever which can prove fatal therefore this study is aimed at analyzing haematological and biochemical parameters for early diagnosis of dengue fever. Thrombocytopenia, leucopenia, increased hematocrit, lymphocytosis with reactive/ atypical/ plasmacytoid lymphocytes along with altered liver function tests are the haematological and biochemical abnormalities that appear in dengue fever.

Hematological and biochemical profile of serologically confirmed 100 dengue cases were done.

Demographic findings and clinical profile: Our study comprised of 55 (55%) males and 45 (45%) females with male to female ratio of 1.4:1.Maximum patients 52 (52%) were in age group of 21-40 years. Mean age was 37.31 + SD17.54 years. Most of theses patients were adults because they form the working age group and more exposure to insect bites. In studies done by Yaseen et al and Shekar et al male to female ratio was 1.4:1 and 1.13:1 respectively[9,10] which was similar to our study. In study done by Ahmed AB et al mean age of the cases was 29.39+ SD10.59 years (range 15 to 69) and almost half of the patients (49%) were in age group of 21-30 years, closely followed by age group of 31-40 years (18.86%)[11] which was similar to our study. This was due to In this study, we found that fever was the commonest symptom in dengue patients, followed by headache/retro-orbital pain (65%) and myalgia (64.15%). Other prominent symptoms were arthralgia, skin rash, skin haemorrhage, loose motion, mucosal bleed and nausea/vomiting. These findings were comparable to those documented by others, though the frequencies of the symptoms varied slightly. In our study, itching, especially in the palms and soles, was noted in 01% of patients which was comparable to similar study by Deshwal R et al[2].

Hematological profile

In our study hematocrit was raised in 06 (06%) cases. Studies done by Gajera VV et al and Butt N et al showed hematocrit values raised in 28% and 50% cases respectively. In studies done by Gajera VV et al and Butt N et al there are more cases of Dengue haemorrhagic fever 30% and 100%[12,13] respectively. While in our study we have early cases of dengue fever i.e. classical dengue fever (98%). Rising hematocrit levels are a marker of the critical phase of dengue infection. The extent up to which hematocrit rises from the baseline can indicate the severity of plasma leakage and progression of disease from dengue fever to dengue haemorrhagic and shock state. In our study thrombocytopenia (Platelets count <1lakh/mm^3) was seen in 54 (54%) cases. Out of which mild

thrombocytopenia (0.5-1 lakh/mm^3) was seen in 38 (38%) cases, moderate thrombocytopenia (20,000-50,000 /mm^3) was seen in 14 (14%)cases and severe thrombocytopenia (<20,000/mm^3) was seen in 02 (02%) cases. While platelet count from 1lakh to 1.5 lakh/mm^3 was seen in 22 (22%) cases and >1.5 lakh/mm^3 was seen in 24 (24%) cases. This was similar to study done by Shekar et al in which thrombocytopenia was seen in 61% cases[10]. While in studies done by Gajera et al and Tahlan A et al platelet count <1 lakh/mm^3 was seen in 81% and 67.39% cases respectively[12,14]. Reason for discrepancy was we were having more early cases of dengue fever as compared to these studies. In study done by Ahmed AB et al Platelet count <1 lakh/mm^3 was observed in 54.7% of the cases. Moderate thrombocytopenia (20,000-50,000/mm^3) and severe thrombocytopenia (<20,000/mm^3) were found in 16.98% and 3.77% of the patients respectively which is very much similar to our study[11]. Bone marrow suppression, immune-mediated clearance and spontaneous aggregation of platelets to virus infected endothelium may be responsible for such thrombocytopenia. Platelet count starts falling from as early as 3rd day of the onset of symptoms and starts recovering by 7th to 9th day of illness.

In our study TLC ranged from 1,500- 14,400 /mm^3. Mean TLC was 4,900/mm^3. TLC <4,000 was seen in 43 (43%) cases and >11,000/mm^3 was seen in 09 (09%) cases. In studies done by Yaseen et al and Gajera et al TLC <4,000/mm^3 was seen in 50% and 39% cases respectively and >11,000/mm^3 was seen in 12% cases which was similar to our study[9,12]. Leucopenia has been reported among dengue patients in many studies. Relative neutrophilia and lymphocytosis was seen in 14(14%) and 40 (40%) cases respectively. Leucopenia is the most prominent haematological change sometimes with counts of less than 2,000/mm^3. However mild leucocytosis with neutrophilia is seen at the onset of the disease developing leucopenia later on. Lymphocytosis was the common finding with the presence of atypical and plasmacytoid lymphocytes on peripheral smear were representative of augmented immune response to control the spread of dengue virus infected cells.

Biochemical profile: The liver is one of the target organs for dengue and clinical manifestations of hepatic dysfunction can occur during the course of this disease. Liver is deprived of oxygen leading to lesions of the parenchyma and injured hepatocytes release transaminases that are detectable in the peripheral blood. In our study AST, ALT, ALP and bilirubin were raised in 64 (64%), 60 (60%), 12 (12%) and 02 (02%) cases respectively. These results are similar to many studies. Study done by Gajera VV et al liver function tests were deranged in 57% of cases while in study done by Yaseen et al AST, ALT, ALP and bilirubin were deranged in 74%, 60%, 09% and 04% cases respectively[9,12].

CONCLUSION

Haemoconcentration, leucopenia, thrombocytopenia, and raised liver enzymes SGOT and SGPT along with reactive/plasmacytoid lymphocytes on peripheral smear gives enough clues to test for dengue serology so that dengue cases can be diagnosed in their initial stages. This facilitates early treatment and aggressive fluid replacement therapy with good nursing care so that fatality rates can be reduced. This would minimize morbidity and mortality arising out of serious complications of dengue fever.

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