



A Retrospective Study in Dengue Positive Cases - Hematological and Biochemical Parameters (Liver Function Tests, Renal Function Tests) Correlation

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ABSTRACT

Dengue fever is the most common arboviral infection in the world, and it is a disease with a broad clinical spectrum and a wide variety of presentations, ranging from asymptomatic to an undifferentiated fever (viral syndrome) to the more severe forms such as severe dengue (SD) or Dengue hemorrhagic fever (DHF). The diagnosis of dengue fever is carried out based on clinical, epidemiological and laboratory data. Among laboratory tests, both non-specific [blood count, platelet count, tourniquet test, prothrombin time (PT), activated partial thromboplastin time (APTT), liver function tests and serum albumin concentration] and specific tests (viral isolation tests and serology for antibody examination) are used. The principle aim of our study is to assess and compare the biochemical and haematological parameters of patients with dengue. In our study population, the peak frequency of the patients who were dengue positive was on the age group between 21 and 30 years (44%), and it was more common among males. The most common serological indicator of dengue fever was the presence of NS1 antibody. High haematocrit (56%) was found in most of the patients, and the next common finding was thrombocytopenia (51%). Elevated Serum glutamic oxaloacetic transaminase seen in 53% of cases and Elevated Serum glutamic pyruvic transaminase, Alkaline Phosphatase, Serum Bilirubin, Serum creatinine and Serum urea were found in 41%, 11%, 7%, 4%, 3% of cases respectively. The knowledge about these parameters helps the clinician in early diagnosis of the cases and initiation of the management measures before the drastic clinical features of the disease sets.



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INTRODUCTION

Dengue fever is the most common arboviral infection in the world (Jameel *et al.*, 2012). Dengue is caused by one of the four serotypes of the dengue virus (DEN-1, DEN-2, DEN-3 and DEN-4) also referred to as an arbovirus (arthropod-borne viruses) that belongs to the genus *Flavivirus* of the family *Flaviviridae*.

The pathophysiological process that occurs in dengue haemorrhagic fever is thrombocytopenia, plasma volume reduction. It is a disease with a broad clinical spectrum and a wide variety of presentations, ranging from asymptomatic to an undifferentiated fever (viral syndrome) to the more

severe forms such as severe dengue (SD) or Dengue hemorrhagic fever (DHF).

Transmission to humans occurs by the bite of the female *Aedes aegypti* mosquito infected by one of four serotypes of the virus. Dengue fever affected more than 100 countries worldwide, with a global at-risk population exceeding 40% (Navinan *et al.*, 2015). WHO estimates 50-100million cases of dengue every year. More than three hundred thousand cases of dengue hemorrhagic fever (DHF) are diagnosed each year, resulting in 24,000 deaths per year (Rashmi, 2015).

The diagnosis of dengue fever is carried out based on clinical, epidemiological and laboratory data. Among laboratory tests, both non-specific [blood count, platelet count, tourniquet test, prothrombin time (PT), activated partial thromboplastin time (APTT), liver function tests and serum albumin concentration] and specific tests (viral isolation tests and serology for antibody examination) are used.

Leukopenia is the most major haematological change, sometimes with counts of less than 2000 cells/cu mm. 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 and is associated with thrombocytopenia ($< 100 \times 10^9/L$).

Of biochemical variables, the most frequent changes occur in liver function tests such as in serum bilirubin, serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), Gamma-glutamyl transpeptidase and alkaline phosphatase levels, and serum albumin concentrations (Iqtadar *et al.*, 2017). Appropriate investigations for evaluation of hepatobiliary dysfunctions were performed (Bandyopadhyay *et al.*, 2016). Varying degrees of liver involvement is seen during acute dengue infection (Fernando *et al.*, 2016). Demographic characteristics and known potential risk factors for acute liver failure were recorded (Laoprasopwattana *et al.*, 2016).

The other frequently changing biochemical variable occurs in renal function tests. One of the crucial indicators is raised serum creatinine level (Mirza *et al.*, 2016).

This study aims to assess and compare the biochemical and haematological parameters of patients with dengue fever to increase the sensitivity of the screening and to identify the laboratory markers which could guide the physician to start specific treatment.

MATERIALS AND METHODS

This is a cross-sectional retrospective study. All cases related to dengue fever sent for analysis to the Department of Pathology, Microbiology and Biochemistry in our institution for two months (November 2018 to December 2018) has been included in this study. All the positive test cases were included for the study, as every reported case contained adequate information. A sample of 100 cases of dengue was analyzed. Dengue infection was diagnosed according to the Case definition described by the WHO guidelines. Data regarding the demographic details of the patient, clinical presentation, haematological parameters, liver function and renal function test results were collected from the hospital records after prior consent from the Head of the Department of the concerned wards. A complete analysis was carried out with the collected data.

RESULTS

This retrospective study was done in our institute in the Department of Pathology with a sample size of 100. All the 100 patients had sent their blood sample for the examination of their haematological parameters to the pathology laboratory. The collected data showed the following findings.

Sex Distribution

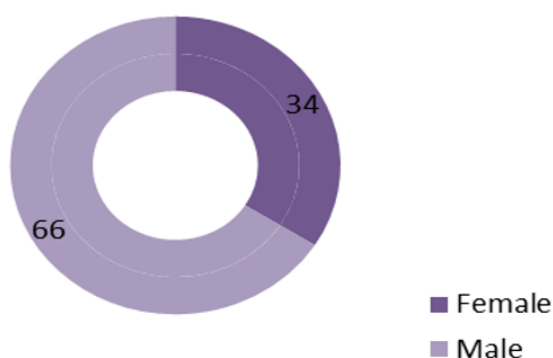


Chart 1: Sex distribution

The peak frequency of the patients who were dengue positive is on the age group between 21 and 30 years (44%), as shown in Table 1.

Among the positive dengue cases, the sex ratio of male to female is in the ratio 2:1. This indicates that the male population is affected twice than that of the female population, as shown in Chart 1.

The most common serological indicator of dengue fever is the presence of NS1 antibody, which is

Table 1: Age distribution of Dengue positive cases.

Age in years	Number of patients (%)
0-10	7
11-20	21
21-30	44
31-40	7
41-50	11
>50	10

Table 2: Spectrum of Hematological Changes

Low Hemoglobin	High PCV	Thrombocytopenia			Leucopenia	Neutrophil	Lymphocytes	Eosinopenia
		Mild	Moderate	Severe				
23	56	28	19	4	33	18	18	42

Table 3: Spectrum of Biochemical Changes

Elevated Serum.Bilirubin	Elevated SGOT	Elevated SGPT	Elevated Alkaline phosphatase	Elevated Serum Urea	Elevated Serum Creatinine
7	53	41	11	3	4

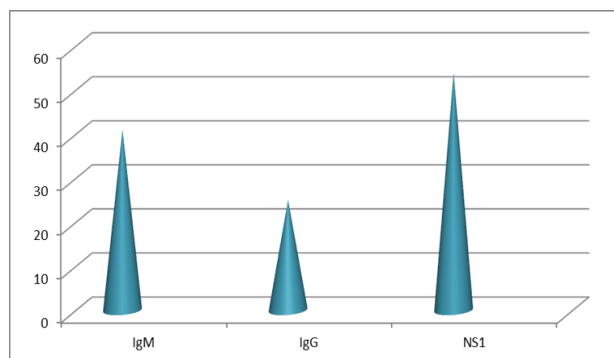


Chart 2: Spectrum of Hematological Changes

present in 54% of the cases. The other common indicators present in the serum are IgM antibody (41%) and IgG antibody (25%) as depicted in Chart 2.

The common haematological changes viewed in the serum of patients are High Packed Cell Volume (56%), Thrombocytopenia (51%), Eosinopenia (42%), Leucopenia (33%), Low Hemoglobin (23%), Neutrophilia (18%), and Lymphocytosis (18%) as shown in Table 2.

The biochemical markers of dengue fever infection from our collected samples are as follows: Elevated Serum glutamic oxaloacetic transaminase (53%), Elevated Serum glutamic pyruvic transaminase (41%), Elevated Alkaline Phosphatase (11%), Elevated Serum Bilirubin (7%), Elevated Serum creatinine (4%) and Elevated Serum urea (3%). This is

shown in Table 3.

DISCUSSION

It is hard to assess the actual prevalence of the disease in the population since many patients present as a flu-like syndrome with spontaneous resolution. Hence, it is not notified entirely (Fernandes et al., 2017). In patients taking high immunosuppressive medications, fever is concealed. This result is under-reporting of the disease, and the diagnosis becomes difficult. Most of the literature describe dengue as a benign disease in the population (Prasad et al., 2012). The mean time of dengue symptoms is higher than the general population. The factors supporting this include the usage of immunosuppressive medications and the prolonged period of viral clearance in those who are immunocompromised (Nasim et al., 2013).

Our study was held in monsoon season. Literature reported the maximum incidence in October and November. The factors contributing to the high number of cases reported in this period are temperature and the humidity present in the environment that facilitates the breeding of mosquito vectors (Hakim et al., 2011).

The age group of 21 to 30 years contributes to the largest proportion of patients affected by the dengue viral infection. Similar age group was reported in the literature (Khan et al., 2010).

The proportion of male sex in the study group is 66% with male to female ratio of 1.9:1. In most of the literature, the male population exceeds the female population ([Achalkar and Kusuma, 2017](#)).

In our study, high packed cell volume is seen in most of the cases (56%), followed by thrombocytopenia (51%) and eosinopenia (42%). The mortality rate is analyzed in some literature ([Azevedo et al., 2007](#)), while this was not discussed in our study since there was no death among the study population. T cells and interleukins mediate the immunopathological process in a severe form of the disease ([Wilder-Smith and Schwartz, 2005](#)). In dengue patients with the subclinical presentation, we must take care of the packed cell volume and thrombocytopenia even before the onset of fever ([Fernandes et al., 2017](#)). Studies have proven decrease in leukocyte count, and lymphocytosis can be seen in dengue infection even in early stages ([Jameel et al., 2012](#)).

Most of the cases developed to be benign without higher mortality. Differential diagnosis of fever and thrombocytopenia must point towards dengue viral infection in patients from regions of high endemicity.

In the current study, the most frequent haematological findings are thrombocytopenia, leucopenia, eosinopenia and an increase in the packed cell volume. There was a presence of reactive lymphocytes in the peripheral blood smear.

The biochemical markers such as serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase were increased in a large proportion of the cases. The three most important parameters helpful in diagnosing a person associated with dengue includes thrombocytopenia, leucopenia and elevated biochemical markers serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase ([Wilder-Smith and Schwartz, 2005](#)). The incidence of thrombocytopenia in this study was 51%. The fall of platelet count is due to reduced functioning of the bone marrow, development of autoantibodies against the person's platelets, direct invasion of megakaryocytes by the dengue virus belonging to the Flaviviridae family. The pathogenesis behind platelet lysis by autoantibodies is through complement activation. There is cross-sensitivity between the antibodies developed against NS1 antigen and thrombocytes. This explains the pathogenic role of the antiplatelet autoantibodies in dengue fever. Thrombocytopenia is a persistent laboratory finding in dengue viral infection, but the absence of thrombocytopenia will not rule out the possible diagnosis of dengue viral infection ([Lei et al., 2001](#)). In the current study,

49% of the patients showed normal platelet count with the positive serological result. There is usual comorbidity of leucopenia in the dengue infected patients. This impairs the T-cell responses in dengue patients ([Dutta et al., 2011](#)).

The hematocrit levels were increased by 56% of the cases in our study group. The peripheral smear examination was done in all the reported cases to rule out spurious thrombocytopenia.

There was a presence of atypical lymphocytes in the collected sample. The incidence of lymphocytosis is only 18% in this study. The incidence of lymphocytosis is associated with impairment in the T-cell response. This triggers the overproduction of autoantibodies and delays viral clearance from the body.

There is an increase in the levels of aminotransferase in 53% of the study population. Serum glutamic oxaloacetic transaminase levels were higher than serum glutamic pyruvic transaminase levels. Dengue virus is hepatotropic. Pathological examination of the hepatocytes reveals the presence of antigens developed in response against the dengue virus. There is an elevation of serum transaminase levels in dengue patients. The degree of elevation corresponds to the level of haemorrhagic episodes in the affected individuals. This has to be taken into consideration while diagnosing a case of dengue haemorrhagic fever.

Regarding kidney function tests, the proportion of patients with elevated serum creatinine is 4%, and the population with elevated serum urea is 3%. The incidence of the cases with altered kidney function test is 27.2% in a study conducted in Brazil. There is evidence of spontaneous resolution to the baseline levels of creatinine, and hence this does not attract clinical significance in the diagnosis of the dengue haemorrhagic fever. The clinician must keep an eye on the biochemical markers on renal parameters such as serum urea, serum creatinine, albumin-globulin ratio, blood urea nitrogen. There can be a requirement of dialysis support to the patients developing acute kidney failure.

CONCLUSIONS

Dengue fever has effects on haematological, hepatological and renal systems in the affected individual. The early detection of dengue viral infection will be based on three main entities, namely thrombocytopenia, leucopenia and elevated levels of serum glutamic oxaloacetic transaminase. The supporting factors include elevated hematocrit levels and atypical lymphocytosis. The knowledge about these

parameters helps the clinician in early diagnosis of the cases and initiation of the management measures before the drastic clinical features of the disease sets. The proper management with appropriate fluid replacement therapy along with supportive measures will bring down the disease-specific fatality rate to 1% or less.

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Conflict of interest

The authors declare that they have no conflict of interest for this study.

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