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A Study of Biochemical and Haematological Parameters in Dengue Patients in a Tertiary Care Hospital in South India

Jocelin Harriate D Almeida[1], Akshaya Kotian[2] and Ankitha Gururaj Bhat[3]*

[1]M.Sc MLT Hematology & Blood transfusion, Lecturer, Department of MLT, Acharya Institute of Allied Health Science, Bangalore, Karnataka, India

[2]M.Sc MLT Hematology & Blood transfusion, Deputy Quality Manager and Asst lab incharge, AJ Hospital and Research Centre, Mangalore, Karnataka, India

[3]M.Sc MLT Microbiology & Immunology, Lecturer, Department of MLT, Acharya Institute of Allied Health Science, Bangalore, Karnataka, India

***Corresponding Author:** Ankitha Gururaj Bhat, M.Sc MLT Microbiology & Immunology, Lecturer, Department of MLT, Acharya Institute of Allied Health Science, Bangalore, Karnataka, India.

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Abstract

Background: Dengue fever has been known for more than a century in the tropical countries. Dengue fever is now the most common cause of arboviral disease in the world, with an estimated annual occurrence of 100 million cases and a mortality rate of 25,000 per year. Dengue is diagnosed by reverse transcription polymerase chain reaction (RT-PCR) and detection of NS1 antigen with corresponding IgM, IgG antibodies by Enzyme immunoassay & Immunochromatographic test. These tests are expensive and may not be available in the periphery. So, the routinely performed hematological parameters and correlation with biochemical parameters will aid in the diagnosis of Dengue Fever.

Objective: To assess the biochemical markers of renal and liver function, and the hematological markers in dengue fever and to assess correlation of biochemical and hematological parameters with severity of dengue fever.

Methods: This was a record - based study. Data of patients (demographic, clinical details) was collected from hospital information system. Hematological parameters: Hematocrit, total blood count, total WBC count, Total RBC count, Platelet count and Biochemical markers of liver function: Total bilirubin, direct bilirubin, indirect bilirubin, total protein, albumin, A\G ratio, ALT, AST and ALP was retrieved from laboratory information system. The collected data were analyzed for frequency, percentage and mean± SD.

Results: The study was carried out on a total of 170 participants, including 115(68%) male and 55(32%) females. Hematological findings like reduced platelet count and raised leucocytes were seen in majority of the cases. Biochemical findings like raised AST and ALT were seen.

Conclusion: Thrombocytopenia, raised total leucocyte count, raised AST and ALT will aid in early diagnosis of Dengue infection. Early recognition and prevention rather than treatment of complications is most important for favourable outcome of the disease.

Keywords: Dengue fever; Thrombocytopenia; Hematological and Biochemical parameters

Introduction

Dengue epidemics are known to have occurred regularly over the last three centuries in tropical, subtropical and temperate areas around the world. The first epidemic of dengue was recorded in 1635 in the French West Indies, although a disease outbreak compatible with dengue had been reported in China as early as 992 AD [1]. The first dengue fever in India was reported during 1956 from Vellore and the first dengue haemorrhagic fever occurred in Calcutta in 1963. In India the annual incidence is estimated to be 7.5 to 32.5 million. All the four serotypes i.e., Dengue 1, 2, 3 and 4 have been isolated in India [2].

Dengue is an acute arthropod-borne viral infection that places a heavy socioeconomic and disease burden on many tropical and subtropical regions, and is the most frequent arboviral disease globally. The incidence of dengue has increased dramatically over the past few decades, and the infection is now endemic in some parts of the world [3]. It is also known as breakbone fever due to the severity of muscle spasms and joint pain, dandy fever or seven-day fever because of the usual duration of symptoms [4].

WHO has estimated that globally, 2.5-3 billion individuals living in tropical or subtropical countries experience dengue transmission. While 50-100 million cases of dengue infection and 24000 deaths tend to occur in 100 endemic countries. Risk of mortality in treated cases of DHF/DSS is 1% while mortality rate among untreated cases may reach up to 20% [5].

Flavivirus belonging to the viral family Flaviviridae causes dengue fever. It is a mosquito-borne, single-stranded RNA virus which is transmitted by the vector Aedes aegypti [3]. It is the fastest spreading mosquito-borne viral disease globally, affecting greater than 100 million humans annually. Dengue also causes 20 to 25,000 deaths, primarily in children, and is found in more than 100 countries. Epidemics occur annually in the Americas, Asia, Africa, and Australia [5].

The WHO estimated that 40% of the global population (Approximately 2.5 billion people worldwide) who live in the tropical and subtropical countries are at risk of getting infected by dengue virus [4, 5]. The human-mosquito transmission cycle occurs primarily in urban environments. And depends on the viral load of the mosquito's blood meal [6]. The period of transmission from humans to mosquitoes begins a day before the start of fever up to the sixth day of illness corresponding to the viremia phase. In humans, the incubation period ranges from 3 to 15 days (intrinsic incubation) with an average of 5 days [6].

Female Aedes aegypti is the primary vector, transmitting the disease to humans. After an incubation period of 4-10 days in the mosquito, the infected mosquito can transmit the virus for the rest of its life. Infected asymptomatic or symptomatic humans are the main multipliers and carriers of the dengue virus and serves as a source for uninfected mosquitoes. Infected patients can transmit the infection via these vectors after their first symptoms appear. Man-made containers containing water act as urban habitat for the Aedes aegypti mosquito. The mosquito is a day-time feeder and its peak feeding period is early in the morning and before dusk. In the breeding habitat, its eggs remain dry for up to a year and capable of hatching when come in contact with water. Aedes albopictus is a secondary dengue vector, especially seen in Asia [6, 7].

Spectrum of clinical presentation of dengue infection ranges from asymptomatic infection to mild self-limiting febrile illness or fatal dengue hemorrhagic fever or dengue shock syndrome. Dengue fever can be classified into three major forms: Dengue fever (DF), Dengue hemorrhagic fever (DHF), and Dengue shock syndrome (DSS). The classic DF is characterized by the symptoms such as petechiae, purpura ecchymosis, gum bleeding and vaginal bleeding, as well as indicators of DHF with plasma leakage, were all deemed DHF. A rapid feeble pulse with a narrow pulse pressure is characteristic of DSS [5]. The clinical presentation of dengue patients is acute febrile illness with no localizing signs and symptoms which may mimic other infections.

Diagnosing dengue early is challenging since the initial symptoms of dengue are often nonspecific and serological tests which are the mainstay of current laboratory diagnosis, confirm dengue late in the course of illness. Currently, the serological test is used to confirm the diagnosis of dengue infection such as the detection of the dengue NS1 antigen (sensitivity 76% and specificity 98%) or the dengue IgM antibody by the ELISA method (sensitivity 90% and specificity 93%) [6]. Nevertheless, these serological tests may be inaccessible in underdeveloped countries or in some smaller hospitals settings, so the clinical clues from the history taking, physical examination,

and routine laboratory tests like CBC and biochemical parameters are still considered as important [7, 8] The CBC in dengue patients changes by the day of the fever, specifically on days 3 to 8, starting with progressive leukopenia followed by thrombocytopenia and hemoconcentration due to plasma leakage [9, 10, 21]. Dengue fever's most dreaded complication is thrombocytopenia which leads to bleeding. Drastic decrease in platelet counts can be used to predict the severity of the disease [9, 22].

Hence the main objective of the current study were to assess the biochemical markers of renal and liver function, and the hematological markers in dengue fever and also to assess correlation of biochemical and hematological parameters with severity of dengue fever.

Materials and Method

Study Setting: Father Muller Medical College Hospital, Kankanady, Mangalore- a tertiary care Hospital, Karnataka, South India.

Study design: Prospective Descriptive Study.

Study Population: Dengue positive patient within the age group of 20-60 years.

Study duration: One year.

Sample Size: The estimated sample size is 167.

Inclusion Criteria

All the adult patients, within the age group of 20-60 years with fever and found positive for Dengue IgM and IgG antibodies assay were incorporated in the study.

Exclusion Criteria

- Patients suffering with other co-infection like Malaria, Typhoid etc. or with any other co morbid conditions like cancer and bleeding disorders.
- Pregnancy, Pediatric, elderly people above 60 years.

Methodology

This was a record - based study. Data of patients (demographic, clinical details) were collected from hospital information system. The laboratory results of following tests were retrieved from laboratory information system.

1. Hematological parameters: Hematocrit, total blood count, total WBC count, Total RBC count, Platelet count
2. Biochemical markers of liver function, renal function: Total bilirubin, direct bilirubin, indirect bilirubin, total protein, albumin, A\G ratio, ALT, AST and ALP. Urea, Creatinine.

Statistical analysis

Numerical Variable analyzed by Mean and Standard Deviation and Categorical variable by Frequency and Percentage.

Sample Size Estimation

$Z_{\alpha}^{2\sigma 2}$

d^2

Zα = 1.96 AT 95% CI

n = σ = Standard deviation

d = 10,000

σ = 65836

n = 167

Results

The study was carried out on a total of 170 participants, including 115(68%) male and 55(32%) females with age range of patient with dengue was 20 to 60 years with the mean age of 34.78 ± 11.35.

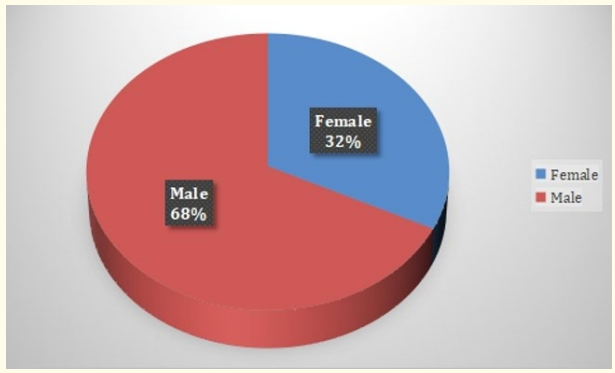

Figure 1: Distribution of gender according to study population.

Parameters	*MEAN*	*SD*
Haemoglobin (g/dl)	14.25	1.94
Total Leucocyte count (/cumm)	40808	3638
Neutrophil count (%)	56	18.07
Lymphocytes (%)	30.2	14.25
Eosinophil count (%)	1.35	1.75
Monocyte count (%)	8.42	4.19
Basophils count (%)	0.05	0.15
Platelet count (/cumm)	71350	60586
PCV (%)	42.27	5.63

Table 1: Distribution of hematological parameters among the study population (N=170).

Parameters	*Minimum*	*Maximum*	*Mean*
Haemoglobin (g/dl)	7	20.5	13.75
Leucocyte count (/cumm)	500	30200	15350
Neutrophil count (%)	4	94	49
Lymphocytes (%)	4	70	37
Esinophil count (%)	0	11	5.5
Monocyte count (%)	0	30	15

Basophils count (%)	0	0.8	0.4
Platelet count (/cumm)	5000	474000	239000
PCV (%)	20.3	56.9	38.6

Table 2: Distribution of hematological parameters among the study population (N=170).

Parameters	***MEAN±SD***
Serum Urea (mg/dl)	20.76±9.37
Serum Creatinine (mg/dl)	0.92±0.25
Serum Total Bilirubin (mg/dl)	0.79±1.49
Serum Conjugated Bilirubin (mg/dl)	0.41±1.29
Serum unconjugated bilirubin (mg/dl)	0.38±0.27
Serum AST (IU/L)	150.8±145
Serum ALT (IU/L)	94.8±82.53
Serum Total Protein (gm/dl)	6.59±0.61
Serum Albumin (gm/dl)	3.92±0.49
Serum Globulin (gm/dl)	2.67±0.44

Table 3: Distribution of biochemical parameters among the study population (N=170).

Parameters	***Minimum***	***Maximum***	***Mean***
Serum Urea (mg/dl)	5	59	32
Serum Creatinine (mg/dl)	0.44	2.74	1.59
Serum Total Bilirubin (mg/dl)	0.16	18.79	9.47
Serum Conjugated Bilirubin (mg/dl)	0.04	16.35	8.19
Serum unconjugated bilirubin (mg/dl)	0.09	2.44	1.26
Serum AST (IU/L)	18	1214	616
Serum ALT (IU/L)	9	664	336.5
Serum Total Protein (gm/dl)	4.67	8.32	6.49
Serum Albumin (gm/dl)	2.1	5.64	3.87
Serum Globulin (gm/dl)	1.5	4.4	2.95

Table 4: Distribution of biochemical parameters among the study population (N=170).

Parameters	***Complicated Dengue (MEAN ±SD)***
Hb	14.16± 2.67
TLC	7757± 6468
PLT	103429± 154271
UREA	25.71±12.53
CREAT	0.8043± 0.17
TB	0.9586± 0.46
AST	218.6± 202.1
ALT	128.1± 77.41

Table 5: Distribution of Complicated Dengue among the study population (N=170).

PARAMETERS	*UNCOMPLICATED DENGUE (MEAN ±SD)*
Hb	14.25± 1.92
TLC	4681± 3444
PLT	69972± 53865
UREA	20.55± 9.21
CREAT	0.93± 0.26
TB	0.78± 1.52
AST	147.9± 142.2
ALT	93.37± 82.66

Table 6: Distribution of Uncomplicated Dengue among the study population (N=170).

Discussion

Being a tropical country, India provides suitable weather for Aedes to grow and an increase in the disease burden has been noticed in recent years. Dengue fever is a self-limiting disease. Dengue hemorrhagic fever causes morbidity and mortality. No antiviral treatment is available hence fluid and electrolyte replacement with supportive therapy are the available modalities of treatment. Since no vaccine is available for the disease, vector control is the only way to check the transmission of the disease.

It is diagnosed by Reverse Transcription Polymerase Chain Reaction (RT-PCR), detection of NS1 Antigen with corresponding IgM, and IgG antibodies by ELISA & Immunochromatographic test. These tests may not be available in the periphery. So, the hematological parameters like platelet count, hematocrit, leucocyte count, and peripheral smear findings will aid in the diagnosis of Dengue Fever.

A study subject with an age range of 16 to 80 years was included in our study.

Study	*AGE (MEAN±SD)*
Our study	34.78 ± 11.35
Dr. Reetu Singhal Resident & Dr. Karan Shrikant Patil [11]	33.12± 14.33
T. T. P. Jayadas et al [12]	30.61±15.06,
Durga Dhungana et al [13]	31.9 ± 12.9

Table 7: Comparison of mean age with various studies.

Thrombocytopenia was a frequent finding in a study by Patel et al [15], Meena et al [14], and Deshwal et al [16], Similar results were found in our study having severe thrombocytopenia in 23% of the dengue-positive cases. They required immediate prophylactic platelet transfusion to prevent any hemorrhagic complications. Thrombocytopenia is due to the direct and antibody-mediated destruction of the platelets and megakaryocytes and also due to the suppression of the bone marrow by the virus.

Study conducted by Rai A et al showed similar reports to our study, The most affected parameters were platelet count (thrombocytopenia in 62.6%) and plateletcrit (reduced in 65.6%). There was a significant correlation of Hemoglobin. Platelet count, Plateletcrit, TLC, Percentage of neutrophil. lymphocyte and eosinophil amongst serological groups [17].

Study conducted by Kumar et al. observed increased hematocrit (>29%), leukopenia (44%) and thrombocytopenia (59%) and concluded hemoconcentration, leukopenia, thrombocytopenia, elevated alanine aminotransferase (ALT), and elevated serum bilirubin were noted, similar report were found in most of the patients in the current study,mainly in the form of increased AST and ALT [18-20].

Conclusion

Early recognition of Dengue infection is crucial in reducing complications and mortality. Haematological markers that assist this early detection include reduced platelet count, elevated hemotocrit, coagulation profile, and abnormal cells in peripheral smear, which are supported by liver function tests and serology.

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Declaration of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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