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Original Research Article

Correlation of clinico hematological profile in confirmed cases of dengue

Fatima Iqbal Maniyar[1]*, Ramesh Chavan[2], Umair ul Basheer[3]

[1]Dept. of Pathology, KLE Academy of Higher Education & Research, Belagavi, Karnataka, India
[2]Dept. of Pathology, Jawaharlal Nehru Medical College (KAHER's), Belagavi, Karnataka, India
[3]Dept. of Anaesthesiology, Shridevi Medical College, Tumakuru, Karnataka, India

Abstract

Background: Dengue Fever is a self - limiting illness which is spread by the bite of Aedes aegypti mosquito. WHO estimates about 50-100 million dengue cases every year. Nearly 300,000 cases of dengue hemorrhagic fever are reported with 24,000 deaths every year. In India dengue fever has become more frequent in the recent years. Diagnosis mainly depends on NS-1 antigen detection and IgM antibody detection.
Aims and Objective: This study aims to assess the correlation between clinical manifestations and haematological profile in the confirmed of dengue. Settings and design: One year hospital based observational study.
Materials and Methods: A total of 120 NS-1 dengue positive cases admitted were analysed and correlated with clinical features, haematological and biochemical findings. Statistical analysis used: Chi-square test or Fisher's exact test and Spearman's correlation coefficient were used. A probability value i.e, 'p' value of equal to or less than 0.05 was considered as significant statistically.
Results: Out of 120 dengue patients, 94 were with dengue fever and 26 with dengue haemorrhagic fever. Common clinical features were fever, arthralgia, myalgia, itching, abdominal pain and rash. The main laboratory findings were thrombocytopenia, raised hematocrit, leucopenia, raised SGPT, SGOT and serum alkaline phosphatase.
Conclusion: Dengue fever continues to be a significant health problem. It is important to correlate clinical examination with laboratory profile in dengue patients to minimize the morbidity and mortality arising out of serious complications of dengue fever.

Keywords: Dengue fever, Dengue haemorrhagic fever, NS-1 antigen and Thrombocytopenia.

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1. Introduction

Dengue is a mosquito borne disease caused by Arbovirus, transmitted to humans by the bite of the female Aedes aegypti mosquito.[1] DENGUE VIRUS (DV) is an enveloped, single stranded RNA virus of the family of Flaviviridae. It consists of four serotypes; DV-I, DV-II, DV-III, and DV-IV. All the four serotypes can cause diseases ranging from self-limiting dengue fever (DF) to severe potentially fatal dengue haemorrhagic fever or dengue shock syndrome (DHF/DSS).[1] About 50 million dengue cases occur annually.[2] In India, epidemics are increasing due to rapid urbanization and deficient water management with improper water storage.[3-5] Early detection of dengue is essential for the subsequent management. Serological tests are widely used but the level of accuracy of these tests depends on the sample collection time. A recent test for early diagnosis of dengue is NS1 antigen detection. These diagnostic immunochromatographic strip kits can be helpful in early diagnosis of dengue and reduce the turn around time.[6] The initial symptoms of dengue are non-specific. Therefore this study aims to correlate clinical examination with laboratory profile in dengue patients to minimize the morbidity and mortality arising out of serious complications of dengue fever.

2. Materials and Methods

This study is a one year hospital based observational study.

*Corresponding author: Fatima Iqbal Maniyar
Email: fatimaiqbalmaniyar@gmail.com

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Any male or female patient admitted in the hospital between January 2018 – December 2018 diagnosed as having dengue fever and confirmed in laboratory (NS 1 positive by rapid antigen test) were included.

A total of 120 subjects were enrolled in the study. Patients having other co-infection interfering with interpretation of laboratory diagnosis, immuno compromised patients and those who were not willing were excluded.

Informed consent was taken by all dengue positive patients. Detailed clinical history was taken along with complete haematological, electrolyte levels and serological investigations. The patients were evaluated for clinical features based on symptoms of fever, arthralgia, myalgia, bleeding disorders, abdominal and retro orbital pain, itching and rash.

The blood count was performed on fully automated haematology analyser (Beckman Coulter). The peripheral smears were stained with Wrights stain.

The biochemical investigations were performed on automated Clinical Biochemistry analyser.

2.1. Ethical approval

Obtained from the Institutional Ethical Committee. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study.

2.2. Statistics

The data achieved was coded and entered into Microsoft Excel. Association between variables was determined using chi-square test or Fisher's exact test and Spearman's correlation coefficient. A probability value i.e, 'p' value of equal to or less than 0.05 was considered as significant statistically.

3. Results

Out of the 120 dengue positive patients, 94 were diagnosed as DF and 26 of the patients were diagnosed with DHF.

3.1. Demographic distribution

In the present study 66% patients were males and 34% were females. The male to female ratio was 1.9:1. Maximum patients (70%) were in age group of 14-50 years.

Table 1: Distribution according to age

Age groups	Number of patients	Percentage
1 – 13 years	19	15.8%
14 – 50 years	84	70%
>50 years	17	14.2%
Total	120	100%

3.2. Clinical profile

Fever was the most common clinical presentation, occurring in all patients on presentation. There was no specific pattern of fever and was usually high grade. Other common features were arthralgia, myalgia, abdominal pain, retro orbital pain and itching. Rash and bleeding from skin (petechiae, purpura) gums and nose was mainly seen in dengue hemorrhagic fever cases. There was no mortality reported.

Table 2: Haemoglobin levels in dengue patients

Parameters	DF (n-94)	DHF (n-26)
Fever	94 (100%)	26 (100%)
Arthralgia	69 (73.40%)	20 (76.92%)
Myalgia	74 (78.72%)	22 (84.62%)
Itching	59 (62.77%)	10 (38.47%)
Abdominal pain	51 (54.26%)	22 (84.62%)
Rash	36 (38.29%)	25 (96.15%)
Retro orbital pain	48 (51%)	10 (38.47)
Bleeding disorder	11 (11.70%)	26 (100%)

3.3. Laboratory profile

The most common hematological abnormalities were thrombocytopenia, raised hematocrit and leucopenia. Leucocytosis was observed in most patients on admission in the first days of the disease, followed by leukopenia from the 4th day of the disease. Low MPV was seen in DHF cases.

3.4. Biochemical profile

Markedly raised serum bilirubin, SGOT, SGPT and Alkaline phosphatase was observed in both DF and DHF cases.
Renal function tests (serum urea, creatinine and uric acid) were with in normal range.

Electrolyte levels showed normal serum potassium and chloride but maximum cases were with hyponatraemia.

Table 3: Distribution of patients according to PCV levels

Investigations	DF (n-94)	DHF (n- 26)
Normal Hb	40 (42.55%)	13 (50%)
Raised Haematocrit	54 (57.44%)	12 (46.16%)
Leucopenia	55 (58.51%)	10 (38.46%)
Thrombocytopenia	94 (100%)	26 (100%)
Low MPV	20 (21.28%)	17 (65.38%)
Raised SGOT	70 (74.47%)	23 (88.46%)
Raised SGPT	69 (73.40%)	19 (73.08%)
Raised ALP	63 (67.02%)	22 (84.61%)
Raised Bilirubin	35 (37.23%)	14 (53.83%)
Hyponatraemia	20 (21.28%)	17 (65.38%)

Platelet count was further divided depending upon severity.

Table 4: Distribution of patients according to MPV levels

Platelet	Number of patients	Percentage
<20,000	22	18.3%
20,000 – 49,999	28	23.3%
50,000 – 99,999	59	49.2%
1,00,000 – 1,49,999	9	7.5%
>1,50,000	2	1.7%
Total	120	100%

Maximum cases had moderate thrombocytopenia with a platelet count between 50,000-99,999 lacs/cumm.

Table 5: Distribution of patients according to total leucocyte count

Clinical features		HB	PCV	MPV	TLC	Platelet
Fever	r	NA	NA	NA	NA	NA
	p	NA	NA	NA	NA	NA
	n	120	120	120	120	120
Rash	r	-.098	-.169	.200	-.054	.409
	p	.286	.065	.028*	.555	.0001*
	n	120	120	120	120	120
Myalgia	r	.133	.160	.083	.085	.130
	p	.148	.080	.370	.353	.182
	n	120	120	120	120	120
Arthralgia	r	-.172	-.057	.078	.042	-.193
	p	.060	.539	.398	.648	.045*
	n	120	120	120	120	120
Itching	r	.000	.168	.104	.023	.077
	p	.998	.067	.261	.800	.427
	n	120	120	120	120	120
Abdominal pain	r	.096	-.049	.323	.075	.090
	p	.299	.599	.0001*	.417	.356
	n	120	120	120	120	120
Retro orbital pain	r	-.020	.004	-.010	-.007	.099
	p	.830	.967	.913	.940	.308
	n	120	120	120	120	120
Bleeding disorder	r	-.119	-.012	.207	-.131	-.541
	p	.196	.895	.024*	.153	.0001*
	n	120	120	120	120	120

r=Correlation Coefficient, p = p value (probability value), n = number of study participants
* = Statistically significant
Interpretation: All the clinical features were correlated using “Spearman’s correlation”.

Correlation coefficient (r) was seen between -1 to +1. A negative ‘r’ value indicated negative correlation and positive ‘r’ value indicated positive correlation. ‘p’ value of less than 0.05 was considered to be statistically significant.

If ‘r’ was less than 0.3 it signified weak correlation, if greater than 0.7 then strong correlation exists between two variables. Fever was present in all the study participants, therefore the correlation coefficient could not be obtained in relation to the haematological findings. Patients with rash showed positive correlations with MPV and platelet which was found to be statistically significant.

Arthralgia showed mild haematological correlation, however the correlation with platelet was found to be statistically significant even though it exhibited weak negative correlation coefficient. Abdominal pain showed a moderate positive correlation (r = 0.32) with MPV and it was found to be statistically significant. Those with bleeding disorders showed a weak positive statistically significant correlation with MPV where as with platelet it showed a moderate negative highly statistically significant correlation.

The **Table 6** depicts the correlation between platelet count and the clinical findings using spearman correlation coefficient. It was observed that the type of fever, arthralgia and bleeding disorder was negatively correlated with platelet count, with correlation coefficients (r) as -0.738, -.193 and -.541 respectively. Among all these findings platelet count was found to be strongly correlated with the type of fever the patient had and bleeding disorder. These were found to be highly statistically significant. (p = 0.0001).

Table 6: Correlation between clinical and haematological findings using Spearman's correlation coefficient

Correlation coefficients	Fever	Type of fever	Rash	Arthralgia	Myalgia	Itching	Abdominal pain	Retro-orbital pain	Bleeding disorder
R	NA	-.738	.409	-.193	.130	.077	.090	.099	-.541
P	NA	.0001	.0001*	.045*	.182	.427	.356	.308	.0001*
N	120	120	120	120	120	120	120	120	120

All other clinical findings i.e., Rash, Myalgia, Itching, Abdominal pain and Retro orbital pain were positively correlated and all of them were found to be statistically significant. ($P<0.05$)

4. Discussion

Early diagnosis of dengue is a challenge as it begins with nonspecific symptoms, like fever, arthralgia and myalgia mimicking those of viral infections, malaria and typhoid which are endemic in the country. Serological tests detect virus late in the course of the disease. Haematological investigations help in rapid and early diagnosis of dengue and also forecast the onset of severe dengue. These investigations are very useful in rural setup having limited resources.

The common age group in the present study was 14-50 years (70%). This is the working class of age group and thus these people are more susceptible to mosquito bites because of occupational exposure.[7-9] Males were 66% and females 34%. The male to female ratio was 1.9:1. Male preponderance was seen which correlated with other studies.[10,11]

In this study, 78.30% cases were diagnosed with DF, 21.70% cases with DHF where as none of the cases showed signs and symptoms of DSS. Hospitals with highly trained staff and resources have reported to have reduced incidence of Dengue shock syndrome.[11,12]

In this study, all 120 patients (100%) presented with fever as the initial symptom along with myalgia in 80% and arthralgia in 74.2% of patients. Less common symptoms were abdominal pain, itching and rash. Bleeding disorder was seen in 37 (30.8%) patients.[7,13] Predominant clinical feature of DHF was fever with myalgia severe arthralgia, bleeding disorder, retro-orbital pain, and rash.[14]

In this study majority of patients (55.0%) showed raised hematocrit level due to hemoconcentration attributed to plasma leakage, indicating hypoalbuminemia. This is an indicator of severity, and is significantly associated with increased risk of DH.[15] Therefore, this parameter may be used as early indicator of plasma leakage and a useful prognostic marker. Thrombocytopenia was seen in 98.3% cases and leucopenia was seen in 54.2% cases, which are in agreement with the findings of other studies.[16-20] Majority of the patients (67.5%) had normal MPV. Thrombocytopenia can be triggered by multiple factors. It can result as a consequence of immune response against platelet which causes the binding of dengue antigens to platelets followed by their immunological destruction, mediated by antibodies.[11] It may also be caused as a result of direct infection of dengue virus on megakaryocytes, which results in increased platelet destruction. In the acute stage of this fever, thrombocytopenia is noted due to the depression of bone marrow.[21]

Leucopenia is caused due to suppression of myeloid series in the bone marrow by dengue virus during the acute phase of the disease.[11]

This study showed raised liver enzymes in dengue patients. Comparable results were seen in studies.[22-24]

The cause for the liver dysfunction is multifactorial and may take place secondary to hypoxia, direct effect of virus or immune mediated damage. Dengue virus directly attacks the kupffer cells and the hepatocytes in the liver. It binds to the receptors while entering the cell and is then taken inside the cell by endocytosis, causing apoptosis of cells.[27,30]

ALP is generally raised in hepatobiliary diseases resulting in cholestasis.[23,31]

All the dengue patients presented with normal serum urea and serum creatinine levels. Similar outcomes were found in other studies as well.[32,33]

Hyponatremia was seen in maximum cases which might be the result of salt depletion, low renal excretion, transient unsuitable antidiuretic hormone or the influx of sodium in the cells leading to dysfunction of sodium potassium pump.[34]

5. Conclusion

The findings of this study highlight significant variations in the clinical profile of dengue fever based on clinical features and laboratory parameters. Clinical features viz. myalgia, arthralgia, rash, abdominal pain, retro orbital pain and itching and laboratory parameters that is platelet count, total count, hematocrit and liver enzymes, showed significant variations and should be correlated for early diagnosis and effective management.

6. Source of Funding

None.

7. Conflict of Interest

None.

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