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STUDYING THE BIOCHEMICAL, HEMATOLOGICAL, AND CLINICAL PROFILE OF SUBJECTS HAVING DENGUE VIRAL INFECTION

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ABSTRACT

Background: One of the most common arboviral diseases affecting large populations globally, is Dengue fever. Increased outbreaks of Dengue are reported in the subtropical and tropical regions on the annual basis. Dengue affects a large population in India with a considerable mortality rate. However, the data concerning the biochemical, hematological, and clinical profile of dengue subjects in India are scarce which is vital for appropriate management.

Aim: The present study aimed to assess the biochemical, hematological, and clinical profiles of the subjects affected by the dengue virus in India.

Methods: The present study assessed subjects affected by the dengue virus in India. For all participants, blood samples were collected and assessed for IgM antibodies specific against dengue using ELISA. Biochemical and hematological parameters were recorded along with the clinical features of included subjects.

Results: The most common clinical feature was fever seen in 100% (n=204) study subjects followed by headache in 87.25% (n=178) study subjects, myalgia in 80.39% (n=164) study subjects, nausea and vomiting in 69.60% (n=142) study subjects, abdominal pain in 59.80% (n=122) study subjects, mucosal bleeding and eye pain in 37.25% (n=76) study subjects. Platelet counts were <140,000 cells/cu mm in 59.80% (n=122) of study subjects. raised lymphocyte counts were seen in 1.96% (n=4) subjects and neutrophil counts were higher ≥1500 cells/cu mm in 84.31% (n=172) study subjects. AST levels were higher with >37 IU/L in 45.09% (n=92) subjects with dengue and the ALT levels were >42 IU/L in 17.64% subjects with dengue infection

Conclusions: The present study, considering its limitations, concludes that assessing the laboratory profile and clinical features in the dengue viral infection-affected area can help physicians assess the likelihood of the infection.

Keywords: Dengue, dengue fever, biochemical tests, clinical profile, hematologic parameters.

INTRODUCTION

Dengue virus infection is an arbovirus disease which is a mosquito-born disease posing a concern and burden on the large population globally with a major impact on the subtropical and tropical regions, and most effective on the semi-urban and urban areas. Nearly 2.5 billion population globally has their lives at risk secondary to dengue fever affecting nearly 50-100 million subjects annually over 100 countries as reported by the WHO (World health organization).[1] Among all the affected subjects, 5 lakh individuals are reported to be severe cases of dengue which lead to approximately 25,000 deaths annually. Dengue is declared an endemic disease in the Western Pacific of the Caribbean, South-East Asia, the Eastern Mediterranean, the Americas, and African regions of the WHO.[2]

Recently, an increase has been reported in the incidence of the dengue virus globally which was attributed to the expansion to new countries. A seasonal increase in the subjects with dengue

virus infection is seen globally including in India where an increase in dengue-affected subjects is seen from May to September when there is an increase in positive dengue subjects reporting to the Outpatient Departments and the Emergency care posing an extra burden on the overburdened Indian health care sector concerning the ward admissions, laboratory assessment, and staffs of the various institutes and hospitals.[3]

The factors attributed to the increasing incidence of dengue with its widespread nature are urbanization rapidly and large populations migrating to urban areas, climate changes, no vector control, and poor hygiene providing areas for mosquitoes to grow. To date, no specific treatment modality is available for treating dengue infection. However, fluid replacement therapy along with early detection provides adequate treatment added with antipyretics and analgesics with appropriate care. Adopting these treatment measures has shown a reduced severity to <1% and 20% lesser mortality in affected subjects.[4]

On clinical presentation of dengue fever, adequate diagnosis and management are dependent on the abnormalities in the laboratory findings and the reported clinical features. The subjects with initial infection by dengue virus are usually asymptomatic or have a non-specific fever state presenting as a state of rash, myalgia, weakness, bleeding tendencies, muscle pain, joint pain, bone pains, severe headache, and/or fever. These clinical presentations are also shared by other diseases including typhoid, kala-azar, and malaria which have a high prevalence in India and further present a challenge to the clinician in adequate disease diagnosis.[5]

Dengue virus has four serotypes and is a single-stranded RNA virus of the arbovirus family and Flavivirus genus. Infection with any of the four serotypes can lead to dengue virus infection. A subject acquires lifelong homotypic immunity after being infected with a particular serotype of the dengue virus.[6] During the endemic phase of the disease, all four serotypes can remain in circulation, and a subject can be affected by as many as four serotypes in a single phase of the endemic and four times making once for each serotype. Previous literature data has reported there is a high risk of severe dengue infection development when a subject is infected with different serotypes. Laboratory tests and clinical features can help in the adequate diagnosis of dengue infection.[7]

Among different laboratory tests, various specific and non-specific tests are used. In specific tests, antibody detection with serology, genomic sequence, and viral antigen tests are used,

whereas, in non-specific tests, serum protein concentration, liver function tests, and hematologic parameters are assessed. In countries like India, where a high seasonal prevalence of Dengue viral infection is reported, the treating healthcare personnel should be aware of common, biochemical, hematological, and clinical presentations of the Dengue infection which are vital in managing the affected subjects and reducing the associated mortality.[8] Hence, the present study aimed to assess the biochemical, hematological, and clinical profiles of the subjects affected by the dengue virus in India.

MATERIALS AND METHODS

The present cross-sectional clinical study aimed to assess the biochemical, hematological, and clinical profiles of the subjects affected by the dengue virus in India. The study population comprised the subjects from the Outpatient Department of the Institute. After the detailed study design was explained to all the participants, written and verbal informed consent was taken.

The inclusion criteria for the study were the subjects who were febrile and were considered to have dengue following the WHO criteria of 2009,[9] the subjects who were willing to study participants, and the subjects confirmed for dengue-specific IgM antibody on serological examination. The subjects having a temperature of $\geq 38^{o}C$ were considered febrile. The exclusion criteria were subjects who did not give consent and subjects who were confirmed for chronic diseases including typhoid fever, kala-azar, and/or pneumonia.

After finally including the subjects in the study, detailed history was recorded for all the participants followed by the clinical examination. The study included a total of 204 subjects from both genders. The demographic data and clinical features were recorded for all the participants following the Getachew F et al in 2018.[10] For assessing the clinical features, a performed structured questionnaire was used. ELISA (Enzyme-linked immunosorbent assay) was used to confirm the diagnosis of dengue infection to assess the IgM antibody which was specific for dengue.

All the routine blood investigations were done for all study participants including the hematological parameters. The hematological parameters assessed were Hct (hematocrit), hemoglobin (Hb), platelet counts, DLC (differential leucocyte counts), and/or TLC (total leucocyte counts) using the automated blood analyzer.

Both thin and thick blood smears were made for the malaria parasite. The biochemical tests done were total protein, BUN for renal function tests, creatinine levels, and ALT and AST for LFT (liver function test) using the automated biochemistry analyzer. For each test, the cut-off value was taken depending on the reference values by the laboratory. Also, for collecting other information, the cases that had IgM antibodies specific to the dengue were reviewed to collect other information such as typhoid, kala-azar, or any other chronic disease.

The data gathered were assessed statistically using the SPSS software version 21.0 (IBM, Armonk, NY). The data were expressed in percentages and numbers.

RESULTS

The present cross-sectional clinical study aimed to assess the biochemical, hematological, and clinical profiles of the subjects affected by the dengue virus in India. The study included a total of 204 subjects from both genders who were suspected to have dengue based on the WHO criteria of 2009. The demographic data of the study subjects are listed in Table 1. The age of the study subjects was within the age range of 1 year to 70 years with 15.68% (n=32) subjects from the age range of 1-15 years and 84.31% (n=172) subjects from the age range of 16-70 years. There were 76.47% (n=156) males and 23.52% (n=48) females in the present study as shown in Table 1.

On assessing the biochemical parameters in the study participants, it was seen that the total protein levels were <6.6 mg/dl in 21.56% (n=44) subjects and were raised, i.e., >6.6 mg/dl in 78.43% (n=160) subjects where the normal range of 6.6-8.7 mg/dl. The BUN for renal function test was ≤23.5 mg/dl in 85.29% (n=174) study subjects and was high i.e., >23.5 mg/dl in 14.70% (n=30) study subjects with dengue which had the normal range of 4.7-23.5 mg/dl. The creatinine levels were raised in 19.60% (n=40) of study subjects with dengue where the normal range was 0.6-1.1 mg/dl, and creatinine levels were normal in 80.39% (n=164) subjects with dengue. For the liver function test, AST was higher with >37 IU/L in 45.09% (n=92) subjects with dengue and was within the normal range of 5-37 IU/L in 54.90% (n=112) study subjects with dengue. The ALT levels were normal within the range of 3-42 IU/L in 82.35% (n=168) study subjects and were>42 IU/L in 17.64% of subjects with dengue infection as depicted in Table 2.

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Concerning the hematological parameters in dengue subjects from the study, it was seen that raised lymphocyte counts were seen in 1.96% (n=4) subjects and were normal in 900-2900 cells/cu mm in 98.03% (n=200) study subjects. Neutrophil counts were higher ≥1500 cells/cu mm in 84.31% (n=172) of study subjects and were in the normal range of 1500-8000 cells/cu mm in 84.31% (n=172) of study subjects with dengue. The hematocrit was >46% in 7.84% (n=16) male subjects of the study and was >44% in 1.96% (n=4) female study subjects, and an overall 9.80% (n=20) study subjects where the normal range in males and females was 38-46 and 35-44%. Hemoglobin levels were ≤13gm/dl in 33.33% (n=68) male subjects and was ≤12gm/dl in 10.78% (n=22) female subjects and in total 44.11% (n=90) study subjects where the normal levels were 13-16gm/dl in males and 12-15gm/dl in female subjects. WBC counts were ≥ 4000 cells/ cu mm in 73.52% (n=150) subjects and were normal 4000-10,500 cells/cu mm in 25.49% (n=52) subjects. Platelet counts were <140,000 cells/cu mm in 59.80% (n=122) study subjects and were ≥140,000 in 40.19% (n=82) study subjects where the normal laboratory levels were 140,000-415,000 cells/cu mm as shown in Table 3.

For the clinical features in the study subjects, the most common clinical feature was fever seen in 100% (n=204) study subjects followed by headache in 87.25% (n=178) study subjects, myalgia in 80.39% (n=164) study subjects, nausea and vomiting in 69.60% (n=142) study subjects, abdominal pain in 59.80% (n=122) study subjects, mucosal bleeding, and eye pain in 37.25% (n=76) study subjects, conjunctival hemorrhage and hepatomegaly in 22.54% (n=46) study subjects, abdominal distension in 14.21% (n=29) study subjects, rashes in 7.84% (n=16) study subjects, and the least common clinical feature was a positive tourniquet test in 7.84% (n=16) study participants with dengue as summarized in Table 4.

DISCUSSION

The present study included a total of 204 subjects from both genders who were suspected to have dengue based on the WHO criteria of 2009. The demographic data of the study subjects are listed in Table 1. The age of the study subjects was within the age range of 1 year to 70 years with 15.68% (n=32) subjects from the age range of 1-15 years and 84.31% (n=172) subjects from the age range of 16-70 years. There were 76.47% (n=156) males and 23.52% (n=48) females in the present study. These demographics in the dengue subjects were comparable to the previous

studies of Amin P et al[11] in 2017 and Roy MP et al[12] in 2017 where authors subjects of comparable gender and age distribution with dengue as in the present study.

The study results showed that for the biochemical parameters, the total protein levels were <6.6 mg/dl in 21.56% (n=44) subjects and were raised, i.e., >6.6 mg/dl in 78.43% (n=160) subjects where the normal range of 6.6-8.7 mg/dl. The BUN for renal function test was ≤23.5 mg/dl in 85.29% (n=174) study subjects and was high i.e., >23.5 mg/dl in 14.70% (n=30) study subjects with dengue which had the normal range of 4.7-23.5 mg/dl. The creatinine levels were raised in 19.60% (n=40) of study subjects with dengue where the normal range was 0.6-1.1 mg/dl, and creatinine levels were normal in 80.39% (n=164) subjects with dengue. For the liver function test, AST was higher with >37 IU/L in 45.09% (n=92) subjects with dengue and was within the normal range of 5-37 IU/L in 54.90% (n=112) study subjects with dengue. The ALT levels were normal within the range of 3-42 IU/L in 82.35% (n=168) of study subjects and were>42 IU/L in 17.64% of subjects with dengue infection. These results were consistent with the previous studies of Syed R et al[13] in 2013 and Mohd Y et al[14] in 2017 where raised levels of liver function test were reported in the subjects having dengue fever by the authors in their respective studies.

The study results also showed that for the hematological parameters in dengue subjects from the study, it was seen that raised lymphocyte counts were seen in 1.96% (n=4) subjects and were normal in 900-2900 cells/cu mm in 98.03% (n=200) study subjects. Neutrophil counts were higher ≥1500 cells/cu mm in 84.31% (n=172) of study subjects and were in the normal range of 1500-8000 cells/cu mm in 84.31% (n=172) study subjects with dengue. The hematocrit was >46% in 7.84% (n=16) male subjects of the study and was >44% in 1.96% (n=4) female study subjects, and an overall 9.80% (n=20) study subjects where the normal range in males and females was 38-46 and 35-44%. Hemoglobin levels were ≤13gm/dl in 33.33% (n=68) male subjects and was ≤12gm/dl in 10.78% (n=22) female subjects and in total 44.11% (n=90) study subjects where the normal levels were 13-16gm/dl in males and 12-15gm/dl in female subjects. WBC counts were ≥ 4000 cells/ cu mm in 73.52% (n=150) subjects and were normal 4000-10,500 cells/cu mm in 25.49% (n=52) subjects. Platelet counts were <140,000 cells/cu mm in 59.80% (n=122) study subjects and were ≥140,000 in 40.19% (n=82) study subjects where the normal laboratory levels were 140,000-415,000 cells/cu mm. These results were in agreement

with the previous studies of Rajesh D et al[15] in 2017 and Spoorti V et al[16] in 2016 where authors reported thrombocytopenia, neutropenia, and leucopenia in subjects with dengue fever infection.

Concerning the clinical features in the study subjects, the most common clinical feature was fever seen in 100% (n=204) study subjects followed by headache in 87.25% (n=178) study subjects, myalgia in 80.39% (n=164) study subjects, nausea and vomiting in 69.60% (n=142) study subjects, abdominal pain in 59.80% (n=122) study subjects, mucosal bleeding, and eye pain in 37.25% (n=76) study subjects, conjunctival hemorrhage and hepatomegaly in 22.54% (n=46) study subjects, abdominal distension in 14.21% (n=29) study subjects, rashes in 7.84% (n=16) study subjects, and the least common clinical feature was a positive tourniquet test in 7.84% (n=16) study participants with dengue. These results were in line with the previous studies of Khan A et al[17] in 2010 and Narayan M et al[18] in 2002 were fever, headache, myalgia, and bleeding tendencies were the most common clinical presentation in dengue subjects.

CONCLUSION

The present study considering its limitations concludes that assessing the laboratory profile and clinical features in the dengue viral infection affected area can help physicians assess the likelihood of the infection. The fever followed by headache and myalgia remains the most common clinical features of the dengue viral infection. Leucopenia, anemia, and thrombocytopenia are common laboratory parameters seen in dengue subjects. These clinical, hematological, and biochemical features are needed to be considered while assessing the subjects with dengue virus infection.

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TABLES

Characteristics	Subgroup	%	N=204
Age range (years)	1-15	15.68	32
	16-70	84.31	172
Gender	Males	76.47	156
	Females	23.52	48

Table 1: Demographic data of the study participants

Parameters	Subgroup	%	N=204)	Normal value
Total protein (mg/dl)	<6.6	21.56	44	6.6-8.7 mg/dl
	>6.6	78.43	160	
BUN (mg/dl)	≤23.5	85.29	174	4.7-23.5 mg/dl
	>23.5	14.70	30	
Creatinine (mg/dl)	≤1.1	80.39	164	0.6-1.1 mg/dl
	>1.1	19.60	40	
AST (IU/L)	≤37	54.90	112	5-37 IU/L
	>37	45.09	92	
ALT (IU/L)	≤42	82.35	168	3-42 IU/L
	>42	17.64	36	

Table 2: Biochemical parameters of the study participants

Hematologic Parameters	Subgroups	%	N=204	Normal value
Lymphocytes (cells/cu mm)	≤2900	98.03	200	900-2900
	>2900	1.96	4	
Neutrophils (cells/cu mm)	<1500	15.68	32	1500-8000
	≥1500	84.31	172	
Hematocrit (%)	Male >46	7.84	16	Male: 38-46
	Female >44	1.96	4	Female: 35-44
	Subtotal	9.80	20	
Hemoglobin (gm/dl)	Male ≤13	33.33	68	Male: 13-16
	Female ≤12	10.78	22	Female:12-15
	Subtotal	44.11	90	
WBC (cells/cu mm)	< 4000	25.49	52	4000-10,500
	≥ 4000	73.52	150	
Platelet count (cells/cu mm)	<140,000	59.80	122	140,000-415,000
	≥140,000	40.19	82	

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Table 3: Hematological parameters of the study participants

Clinical features	%	N
Hepatomegaly	22.54	46
Conjunctival hemorrhage	22.54	46
Torniquet test	7.84	16
Rash	12.74	26
Nausea and vomiting	69.60	142
Abdominal pain	59.80	122
Mucosal bleeding	37.25	76
Myalgia	80.39	164
Eye pain	37.25	76
Headache	87.25	178
Abdominal distension	14.21	29
Fever	100	204

Table 4: Clinical features in the study subjects having dengue