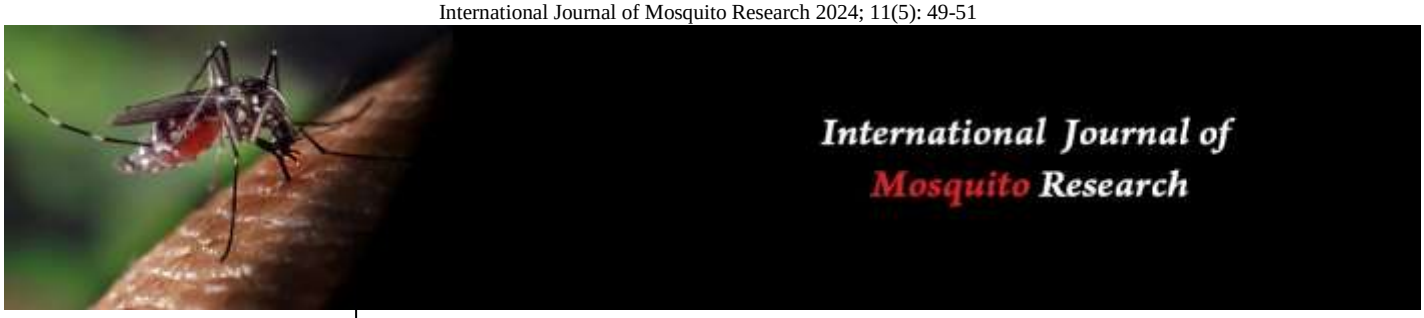

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A study to assess the clinic epidemiological features of dengue virus infection and correlation with serum ferritin levels

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Abstract
Aim: The aim of the present study was to assess the clinic epidemiological features of dengue virus infection and correlation with serum ferritin levels.
Methods: The study was conducted in the Out-patient Department and in patient Department newly diagnosed or suspected 100 adults and children were included for the period of 2 years.
Results: Out of the studied cases, 60% were male and 40% female. Age 20-29 makes approximately 32% of the population. 10–19-year-olds make up 23% and 30–39-year-olds 22%. Diabetes was the second most prevalent co-morbidity in 10 individuals after hypertension (32). Other co-morbidities include hypothyroidism, HIV reactivity, COPD. There was fever in all patients. More over half were hospitalised with fever. The average admission day for patients with fever was 4.6±1.8 days, and the average subsidence day was 5.08±1.62. Our dengue patients' fevers last 3.5–6.5 days. The average hospital stay was 5.7±2.5 days. Mann Whitney's Test determined p values. The average ferritin levels differ considerably between DENV 1 and 2. Though quantitatively greater, DENV 1 serum ferritin is not significantly different from previous infections.
Conclusion: Dengue virus may affect every bodily system and cause any symptom. This notion would assist raise suspicion since early diagnosis and hydration are needed to avoid complications. Dengue fever lasts 5-6 days but might last 8 days. This requires strong judgement before changing diagnoses. Serum ferritin predicts severity well.

Keywords: Clinic epidemiological, dengue virus infection, serum ferritin levels

Introduction
Aedes aegypti and Aedes albopictus mosquitoes disseminate a viral infection known as dengue, which poses a significant health threat in numerous areas [1]. Roughly 50-100 million new infections globally are reported by the World Health Organization (WHO), with 50, 000 cases of severe dengue needing hospitalization and causing death in roughly 2.5% of victims [2]. The incidence of cases has escalated nearly eight-fold over the past two decades, rising from 505, 430 cases in 2000 to approximately 5.2 million in 2019. In 2012, the WHO acknowledged it as "the most consequential viral disease transmitted by mosquitoes" [3]. The case fatality rate of dengue fever in certain rural areas of India ranges from 3% to 5% [4]. Notwithstanding its straightforward and cost-effective management, the fever can become life-threatening if not diagnosed in its early stage. Dengue is well-known to induce significant cytokine activation.
Different dengue virus (DV) serotypes I-IV generate symptoms ranging from asymptomatic infection to severe dengue. Dengue fever is suspected when a febrile illness lasting two to seven days involves two or more symptoms such as headache, retro-orbital discomfort, muscle pain, joint pain, rash, and hemorrhagic presentation [5]. For the first five days of fever, NS1 antigen reactivity by enzyme-linked immunosorbent assay (ELISA) technology is employed to identify dengue fever. NS1 exhibits a diagnostic sensitivity exceeding 90% within two to three days of illness. However, the sensitivity slowly reduces, and it lowers substantially after the fifth day [6]. Dengue virus-specific IgM may be identified and utilized to diagnose DV with excellent sensitivity and specificity. Those who have never been infected with dengue virus

have a sluggish IgM response that rises by 50% after three to five days, 80% after more than five days, and 100% after 10 days [7, 8]. Severe dengue is characterized as dengue hemorrhagic fever and dengue shock syndrome by WHO [9]. Since the severe type has no particular cure, early discovery and good medical care might cut the death rate to below 1%. As a consequence, many biomarkers for immunological and endothelial cell activity have been created to predict the severity [10].

Dengue infection induces an increase in acute-phase reactants such as alpha1 antitrypsin, ceruloplasmin, and ferritin. The reticuloendothelial system generates ferritin, an iron storage protein complex of isoferritins. The clinical effect of depriving bacteria of serum iron is reflected in higher levels of serum ferritin, an acute-phase reactant [11]. Hyperferritinemia in dengue-infected patients is connected to significant immunological activation and coagulation difficulties. Earlier research has demonstrated a link between serum ferritin and the result (Lower serum ferritin levels corresponding with better outcome). The serum ferritin levels have been associated to severe dengue fever in children [12].

The purpose of the current research was to investigate the clinic epidemiological aspects of dengue virus infection and connection with serum ferritin levels.

Materials and Methods

The study was conducted in the Out-patient Department and in patient Department newly diagnosed or suspected 100 adults and children were included for the period of 2 years.

Inclusion criteria:

1. Confirmed Dengue patients (NS1 or IgM reactive by ELISA technique from the Department of Microbiology)
2. Patients who are willing to participate in the research

Exclusion criteria

1. Those who were unwilling to participate in the study.
2. Patients with concurrent bacterial / viral / parasitic infection.

Methodology

A patient suspected of having dengue, who attended the outpatient department and was subsequently admitted to the inpatient department, was evaluated for inclusion and exclusion criteria and was accepted as a case. A comprehensive history was obtained and clinical characteristics were documented. Confirmation of Dengue infection was achieved through NS1 testing (within 5 days of fever) or Ig-M reactivity (after 5 days of fever) via the ELISA method from the Department of Microbiology. On the first day of observation, blood samples were collected for a regular complete hemogram, liver function tests, lipid profile, and renal function tests, conducted by the Department of Biochemistry and Laboratory Medicine, STM. In accordance with the patient's management requirements, additional samples were dispatched for the assessment of various parameters, including complete hemogram, liver function tests, and renal function tests. All data were accurately documented. Serum ferritin measurement was done using ELISA technique.

Results

Out of the studied cases, 60% were male and 40% female. Age 20-29 makes approximately 32% of the population.

Table 1: Demographic data

Gender	N	%
Male	60	60
Female	40	40
Age groups in years		
10-19	32	32
20-29	23	23
30-39	22	22
40-49	11	11
50-59	7	7
60-69	4	4
70-79	0	0
80	1	1
Co-morbidities		
Hypertension	32	32
Diabetes	10	10
Hypothyroidism	7	7
HIV	3	3
COPD	2	2

10–19-year-olds make up 23% and 30–39-year-olds 22%. Diabetes was the second most prevalent co-morbidity in 10 individuals after hypertension (32). Other co-morbidities include hypothyroidism, HIV reactivity, COPD.

Table 2: Other features

Clinical features	
Fever	100
Average day of fever	4.6±1.8 days
Average day of illness	5.08±1.62
Average duration of hospital	5.7±2.5 days

There was fever in all patients. The average admission day for patients with fever was 4.6±1.8 days, and the average subsidence day was 5.08±1.62. Our dengue patients' fevers last 3.5–6.5 days. The average hospital stay was 5.7±2.5 days.

Table 3: The serum ferritin estimated in different serotype infection

	DENV 1	DENV 2	DENV 3	DENV 4
DENV 1	X	0.0070	0.1455	0.1810
DENV 2	0.0070	X	1.0	0.1978
DENV 3	0.1455	1.0	X	0.4286
DENV 4	0.1810	0.1978	0.4286	X

Table 4: Significance study of Ferritin values in different Serotype Infection

Serotype	Ferritin
DENV 1	695±470
DENV 2	1484±733
DENV 3	1468±406
DENV 4	1204±860

The significance or p-values were determined using the Mann-Whitney Test. There is a considerable variation in the average ferritin levels between DENV 1 and DENV 2. Despite being numerically elevated, there is no significant difference in serum ferritin levels between DENV 1 and other types of infections.

Discussion

Dengue is a viral illness disseminated by mosquitoes. The pathogenesis of the disease and the extent of the issue encompass the characteristics of the agent (Dengue Virus -

DENV), vector (primarily Aedes mosquito), host (humans), and the environment. The dengue virus is a little RNA virus, about 50 nm in diameter, classified under the genus Flavivirus and the family Flaviviridae. The genome comprises single strand positive sense RNA of 11644 nucleotides that encodes for 3 structural (C-core, M- membrane and E- envelope) and 7 non-structural (NS1, NS2A, NS2B, NS3, NS4A and NS4B) proteins [13]. Infection with a certain serotype may provide cross-protection against infections by other serotypes for a duration ranging from a few months to two years, and provides lifetime immunity against the same serotype [14-16].

The age group of 20 to 29 years is 32% of the overall population. The 10-19 years age group constitutes 23%, while the 30-39 years age group accounts for 22%. In contrast, Sarkar *et al*. [17] discovered in a 2011 research that the predominant age group affected is 0-10 years. Among the examined patients, 60% were male and 40% were female. In the majority of research, males are marginally and insignificantly more prevalent. Notably, a study conducted by Sarkar *et al*. from ICMR and another from Kolkata identified a predominance of female patients [18]. Hypertension was the predominant co-morbidity identified in the patient population, affecting 32 individuals, while diabetes was the second most prevalent, impacting 10 individuals. Additional comorbidities encompass hypothyroidism, HIV reactivity, and COPD. All individuals had a history of fever. The majority of patients were admitted with fever. The average day of fever in which patients was hospitalized was 4.6±1.8 days and the average day of sickness in which the fever reduced was 5.08±1.62.

The fever in our dengue patients typically lasts from 3.5 to 6.5 days. The mean duration of hospitalization was 5.7±2.5 days. The significance or p values were computed using Mann Whitney's Test. The variation in average value of ferritin is evident considerably between DENV 1 and 2. Though numerically increased there is no significant difference between serum ferritin of DENV 1 and other kind of infection. The research done by Soundravally *et al*. [19] completed the test of serum ferritin in the day of admission as well as on the day of defervescence. They also observed that the value was greatly enhanced in both instances between severe and non-severe dengue as they classed the sickness into two categories. They found that ferritin value higher than 866.5 ng/ml was considerably sensitive and specific (86.9%, 83.3%) to identify the severity. But another research from Thailand by Chaiyaratana *et al*. [20] reported that ferritin value may substantially predict the severity of dengue fever from day 5 to day 7 with a best cut off of 1200 ng/ml which was closer to our findings.

Conclusion

Dengue virus infection can manifest in various forms and exhibit symptoms associated with any bodily system. This concept would undoubtedly facilitate early diagnosis and management of suspicion, as hydration is essential to avert any complications. Dengue fever typically lasts for 5 to 6 days, however it may extend up to 8 days. This requires careful consideration before to pursuing an alternative diagnosis. Serum ferritin is a reliable indicator for predicting severity. The values upon admission markedly varied across the three severity categories. It may thus serve as a proxy for forecasting the progression of the condition.

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