ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

Study on the pattern of changes in biochemical and haematological profiles in dengue-positive patients admitted to tertiary health care hospital Puri on the first, third, seventh, and tenth days of their illness.

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Abstract:
The objective of this research was to establish diagnostic and staging criteria for dengue in order to assist in the most effective treatment of the illness. This was accomplished by taking into account the influence that dengue infection has on a variety of biochemical and haematological markers in individuals who have dengue. Using a cross-sectional technique, a study was carried out at the Shri Jagannath Medical College and Hospital (SJMCH) in Puri. The research investigated the relationship between the two variables. After a clinical suspicion of SJMCH was established, serological testing revealed dengue-specific antigens and antibodies in fifty of the patients. For this study, 50 individuals with febrile diseases of known origin (FKO) other than dengue were chosen as controls. In both cases and controls, the frequency of distinct clinical symptoms, as well as alterations in haematological and biochemical markers, were ascertained. The participants' average age was 34.3 ± 14.4 years, with 12 females and 38 males. Dengue was primarily characterized by fever and headache, which accounted for 100% of cases. There were additional reports of myalgia (82%), retro-orbital discomfort (70%), bleeding tendencies (40%), rash (53%), and vomiting (50%). Leukopenia (64 per cent), hyponatremia (53%), hypokalemia (42 %), hypocalcemia (83%), and thrombocytopenia (92 per cent) were the symptoms that dengue patients had. Vertigo, rash, retroorbital discomfort, and bleeding tendencies were more common in dengue fever patients. Elevated transaminase, urea, creatinine, thrombocytopenia, leukopenia, and aberrant hematocrit levels are often associated with a severe form of the condition, along with reduced blood levels of albumin, cholesterol, salt, potassium, and calcium.

Keywords: Dengue fever, Fever of Known Origin, Hematocrit Value, Hypokalemia, Hypocalcemia, Hyponatremia, Leukopenia.

INTRODUCTION:

Dengue fever is a global issue due to its rapid expansion over more than 125 tropical and subtropical nations with perfect temperatures and population booms. In India, the public's health is in danger from dengue fever, an infectious disease spread by mosquitoes [1]. This arthropod-borne disease is spread over the Indian subcontinent by the Aedes aegypti mosquito.[2]. The virus that is responsible for dengue fever is a member of the family of viruses that is referred to as the Flaviviridae. Due to the fact that there are four distinct serotypes of the virus, individuals are at risk of contracting infections that may continue for the rest of their lives: DEN-1, DEN-2, DEN-3, and DEN-4. [3]. The Aedes aegypti mosquito, which is prevalent in both urban and semi-urban regions, is the primary vector of the illnesses that are responsible for the diseases that cause the sickness. Urbanization and population growth have created an environment that is favourable to mosquito reproduction and increased human-mosquito contact, which is the reason behind the rise in dengue fever in India [4]. Dengue fever outbreaks have been sporadic in recent years, causing a significant amount of disease and fatality in India. Among the symptoms linked to this condition include fever, headache, rashes, muscle and joint pain, and bleeding [5]. In spite of the fact that dengue infection is exceedingly rare, both dengue shock syndrome (DSS) and dengue hemorrhagic fever (DHF) have the potential to result in serious consequences because of their severity. [1-3]. The fact that dengue fever's geographic spread varies so frequently makes managing the disease in India more difficult. Both urban and rural residents of all ages are at risk of getting the disease [4]. States with large populations that have regularly witnessed an upsurge in dengue infections include Uttar Pradesh, Delhi,

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

and Maharashtra [5]. However, the fact that the disease has migrated to low-risk areas emphasizes the need for an all-encompassing and flexible response to halt its spread [7]. Several factors complicate the management of dengue in India. Numerous environmental variables, including urbanization, inadequate water storage, climate change, and poor sanitation, all contribute to the spread of illnesses and the growth of mosquito populations [8]. It is more difficult to control and mitigate dengue fever when there is an erroneous diagnosis, insufficient case reporting, and low public awareness. Dengue fever (DF) has a substantial risk [9]. As a result, several other health organizations, as well as the Indian government, have put control and prevention measures in place [10]. Programs to manage vectors, increase public knowledge, and promote community involvement in the removal of reproductive grounds are also included in this category [11]. Researchers are trying to develop effective immunizations and antiviral drugs to decrease the effects of the disease [12]. As a result of this, dengue fever has developed into a substantial public health problem in India, necessitating the establishment of a comprehensive strategy to manage the sickness and reduce the impact it has on both individuals and communities. In order to preserve the health of the general population, politicians, members of the general public, and medical experts must collaborate in order to put a stop to the development of this illness, which is transmitted by mosquitoes and is growing more prevalent throughout the country [1–5]. In order to monitor the effects of dengue infection on clinical, haematological, and biochemical markers in patients during the first, third, seventh, and tenth days of dengue fever, large-scale research was conducted at a major tertiary care hospital. The study was conducted in order to track the impact of dengue infection. This action was taken due to the prevalence of the condition throughout the nation and the previously cited literature. Determining the severity of an illness and keeping track of a patient's health might be made easier when statistically significant changes in haematological and biochemical markers are present.

MATERIALS & METHODS:

In particular, this study was carried out at the Shri Jagannath Medical College and Hospital (SJMCH) in Puri. A blood sample was taken from 150 people who were suspected of having dengue. Fifty individuals with febrile illnesses of known origin (FKO) other than dengue were studied in order to provide controls for the blood samples.

The current investigation included patients with acute febrile illness lasting two days or more and exhibiting two or more of the following symptoms if they were suspected of having dengue [1,4]. Headache, myalgia, retroorbital pain, rash, bleeding manifestation, or leukopenia were among these symptoms.

The experiment was not open to patients with a documented bacterial infection, any other specific chronic illness, or both. Individuals who had negative IgG tests were excluded from the research.

A plan for gathering information: For every one of the fifty suspected patients and fifty control samples, a complete set of demographic data was collected. The patient's name, age, gender, number of feverish days, prior history of dengue fever, and location were all included in this data. Informed permission was given by the controls and patients in this study to take part in the research. To perform haematological, biochemical, and diagnostic tests, twenty millilitres of blood were extracted from each participant and divided among three different vacutainers. Serum samples that were separated from blood samples centrifuged for biochemical and diagnostic purposes were kept for a further week at 40 degrees Celsius before being examined. On the same day as the other parameters, the haematological parameters were assessed.

Both dengue-specific IgG/IgM antibodies and nonstructural protein 1 (NS1) antigens were used in the in vitro testing of blood samples taken from the patients to determine the presence of dengue malaria. It is thus possible to find dengue infections. This was done by the use of traditional laboratory procedures as well as an immunochromatographic test (ICT) that was performed using the SD BIOLINE Dengue Duo Rapid Test Dengue Diagnostic Kit (Standard Diagnostic Inc.; Seoul, Korea). In addition, an enzyme-linked immunosorbent assay (ELISA) was carried out using kits that are readily accessible for purchase, consisting of NS1 antigen, IgM, and IgG antibodies (Diagnostic Auto). It was determined that each sample was analyzed in line with the directions that the manufacturer supplied.

Blood samples that were serologically positive and identified by ELISA and ICT were categorized into three different groups: DF, DHF, and DSS, in line with the World Health Organization's (WHO) categorization method. These categories were then included in upcoming evaluation processes (World Health Organization, 1997).

Blood-related metrics include the following: Using the haematology analyzer Sysmex KX-21, which was produced in Lincolnshire, Illinois, United States of America by Sysmex America Inc., we determined the

ISSN: 0975-3583, 0976-2833 VOL14, ISSUE 12, 2023

hematocrit (HCT), packed cell volume (PCV), total leukocyte count (TLC), and platelet count (PT) of blood samples acquired from dengue patients.

Listed below are some of the biochemical factors: Albumin, bilirubin (Bili), alkaline phosphatase (ALP), and alanine transaminase (ALT) were the biochemical indicators that were evaluated by the use of the liver function test (LFT). Renal function tests, often known as RFTs, were used in order to detect levels of urea and urea acid. In terms of the lipid profile, the values that were predicted were triglycerides (TG), cholesterol, high-density lipoprotein cholesterol (HDL), very low-density lipoprotein cholesterol (LDL), and low-density lipoprotein cholesterol (LDL). It was determined that measurements of cardiomyocyte enzymes were necessary in order to compute the cardiac profile. In this category were the enzymes known as creatine phosphokinase (CPK), lactate dehydrogenase (LDH), and creatine kinase-MB (CK-MB). In addition, the amounts of sodium, potassium, calcium, and phosphorus in the serum were measured throughout the experiment. In order to determine the levels of calcium and phosphorus that were present in the blood, Beckman Coulter Inc.'s AU kits, which are located in Brea, California, United States of America, were employed. For the purpose of evaluating the potassium and sodium electrolytes, we also used the ion-selective electrode method and the EasyLyte analyzer, which was manufactured by Medica Corporation and located in Bedford, United States. It was determined that the electrolyte concentrations in the serum could be determined using any of these two approaches. An automated chemistry analyzer (Beckman Coulter AU 480; Beckman Coulter Inc., Brea, California, United States of America) and the standard AU reagent were used in order to ascertain the biochemical parameters. This was done in accordance with the instructions provided by the manufacturer.

Statistical Analysis:

Version 21 of the SPSS program was used in order to carry out the statistical analysis. On the other hand, categorical variables are shown via the use of frequencies and percentages and continuous variables are characterized through the use of implies and standard deviations. The chi-square test and Fisher's test were used in order to investigate the connection that exists between the clinical manifestations of dengue fever and the severity of the disease. A statistical technique known as analysis of variance (ANOVA) was used in order to investigate the connection that exists between the haematological and biochemical markers and the severity of dengue fever. When it comes to statistical significance, a threshold of 0.05 was established.

RESULTS:

In this study, a serological investigation was performed on blood samples taken from fifty patients who were suspected of having dengue infections and fifty healthy controls. Patients ranging in age from 12 to 72 years old made up the study population, with the average age being 34 years old. The age range of the patients was rather wide. The total number of incidences that took place between the ages of 12 and 32 was fifty. One hundred and eleven of the patients who were diagnosed with dengue were between the ages of 53 and 72, while forty-six of the patients were between the ages of 33 and 52.

Clinician values for various parameters

The patients reported a wide range of clinical symptoms, including chills, headache, fever, arthralgia, myalgia, vomiting, diarrhoea, and maculopapular dermatitis. Upon reviewing the patient's symptoms, it was discovered that every single one of them had come to the hospital complaining of discomfort and having a temperature. A significant increase in the occurrence of symptoms, such as myalgia, arthralgia, retroorbital pain, chills, stomach discomfort, rash, vomiting, and bleeding, was seen in patients who were treated with DF on the first, third, seventh, and tenth days of their illness (Table I).

Table 1. Clinical parameters observed in dengue fever (DF) patients on the first, third, seventh, and tenth days were compared.

Symptoms	Number of Dengue patients (n=50)	First day	Third day	Seventh day	Tenth day	Control Patients (n= 50)	P Value
Fever	50	50	50	49	01	50	----
Myalgia	42	42	42	40	04	10	< 0.05
Headache	50	50	50	48	01	22	----
Chills	44	44	44	44	00	13	>0.05
Retro-orbital Pain	38	38	38	36	01	6	< 0.05
Abdominal Pain	24	24	24	20	00	6	< 0.05
Arthralgia	43	43	43	40	04	8	< 0.05
Hemorrhagic	9	9	46	38	8	0	< 0.05

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manifestations							
Rash	27	27	27	24	00	0	< 0.05
Vomiting	26	26	26	22	00	8	< 0.05

In comparison to the control group, dengue patients' hematocrit levels were noticeably higher. Patients with DSS had the greatest mean HCT level. In this investigation, 17 males and 5 females had excessive HCT levels (>45%). In 12 males and 8 females, there was a frequency of less than 42% for HCT. The two haematological conditions most commonly seen in dengue patients were leukopenia (leucocyte count fewer than 4,000 cells/µL) and thrombocytopenia (platelet count less than 100,000 cells/µL). 42 individuals in the DF group had moderate thrombocytopenia (platelet count >50000 cells/µL). In contrast, eight patients had severe thrombocytopenia (platelet count <25,000 cells/µL) on the seventh day. Table 2 clearly illustrates the variance in haematological parameters across patients with DF on the first, third, seventh, and tenth days of dengue fever.

Table 2: Various haematological parameters observed in dengue fever (DF) patients on the first, third, seventh, and tenth days were compared.

Symptoms	Number of Dengue patients (n=50)	First day	Third day	Seventh day	Tenth day	Control Patients (n= 50)	P Value
Hemoglobin (g/dL)	12.9 ± 2.1	12.7 ± 2.1	12.1 ± 1.2	14.8 ± 3.4	15.1 ± 1.8	13.8 ± 1.91	> 0.05
Hematocrit (HCT, %)	42.4 ± 5.9	42.4 ± 5.9	38.3 ± 6.7	41.2 ± 7.9	34.5 ± 5.3	35.3 ± 6.3	< 0.05
Total leucocyte (cells/µL)	3489 ± 812	3489 ± 812	4487 ± 1012	3891 ± 984	2892 ± 863	7034 ± 1438	< 0.05
Platelet count (cells/µL)	82451 ± 21302	82451 ± 21302	40342 ± 9134	19784 ± 4128	16687 ± 8876	3247891 ± 10126	< 0.05

Biochemical variables

In the dengue groups, serum albumin and total protein concentrations were substantially lower. However, the levels of transaminases (AST and ALT) were significantly higher. Based on the high AST/ALT ratio, these clinical studies were able to differentiate dengue infection from acute hepatitis caused by hepatitis A, B, and C viruses. According to Table III, there was a correlation between the severity of the disease and higher levels of urea and creatinine concentrations. Significant differences were seen in the levels of cholesterol, LDL-c, and HDL-c in the experimental group and those in the control group. There was a correlation between the severity of the sickness and a persistent reduction occurring in these levels.

Conversely, elevated triglyceride levels were discovered, and they increased in direct proportion to the illness's severity. The dengue group had significantly greater cardiac enzyme levels (CK, CK-MB, and LDH) than the control group due to myocardial cell damage caused by dengue infection. Individuals with DHF and DSS had estimated concentrations of Na+, K+, and Ca++ much lower than those of control individuals.

DISCUSSION:

The purpose of this study was to monitor the clinical manifestations and changes in haematological and biochemical markers among dengue patients living in the Puri region throughout the first, third, seventh, and tenth days of the disease by evaluating the severity of dengue fever (DF). Adolescents and young adults (ages 12-52) had a much higher prevalence of dengue fever than the geriatric group, which was comprised of those aged 52 to 72. Within this age range, there was an increased risk of sickness among young people because they were more likely to participate in outdoor activities and because there were more people engaged. Further studies on persons diagnosed with dengue have provided additional evidence to support the hypothesis that dengue severity is higher in younger age groups than in older age groups [9, 10]. Between the months of August and November, the overall number of patients increased significantly. Dengue fever is more common during the monsoon and post-monsoon seasons because there are more places for mosquitoes to lay their eggs. This outcome was consistent with other research groups' findings [9, 11].

This study looked into the disparities in dengue infection rates between males and females. In this area, male workers are frequently more vulnerable to mosquito bites than female workers. This is a result of the fact that male employees work outside longer than female employees. The results of the present study were corroborated by a number of additional studies [12, 13]. However, studies have indicated that dengue infection is more common in populations with either an equal proportion of males and females or a higher female-to-male ratio

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[14]. Our study revealed that 75% of the patients were classified as DF, which is higher than previous studies' findings that 70% of patients had classic DF [15, 16].

The most often reported clinical symptoms, according to the study's findings, were fever, headache, myalgia, and arthralgia. The results of this investigation agree with those of earlier experiments. [17, 18].

Severe dengue variations have been linked to clinical signs, including petechiae, persistent regurgitation, extreme stomach pain, and bleeding. Previous study has provided support for these conclusions [19].

Additionally, it was demonstrated that there was a connection between increased vascular permeability and plasma leakage, which caused dengue patients' hematocrit levels to rise. Previously, a 22% increase in the hematocrit concentration was identified as the diagnostic threshold for DF. It should be highlighted, nonetheless, that the study's findings regarding the rise in hematocrit levels were significantly smaller than those that were anticipated. Similar results, however, with a lessened increase in the hematocrit, have been seen in other studies [19, 20]. A thorough set of modified guidelines is required on the use of the hematocrit rise in dengue diagnosis. The two most frequently reported symptoms among dengue patients were thrombocytopenia and leukopenia [21]. This is because these symptoms were brought on by the bone marrow being suppressed and the dengue antigen attaching to platelets. The total leukocyte count and platelet count showed considerable change according to the level of dengue infection.

It was discovered that thrombocytopenic haematological abnormalities affected 92% of the participants. As per the results of prior publications [22, 23], the present findings align with the stated 82% and 92%. Additional research from an Indian group revealed that dengue infection was linked to hemoconcentration, leukopenia, and thrombocytopenia [24]. This study found that increased transaminase levels were present in 94% of dengue patients. According to earlier research, 86, 97, and 97.5% of patients with a dengue diagnosis had elevated levels of transaminases [24, 25, 26]. The information presented here is consistent with such conclusions. Sixty-four per cent of subjects in a Brazilian study had elevated transaminase levels, which is a comparatively small percentage [27].
In contrast to the pattern observed in viral hepatitis, serum AST/ALT levels are often elevated in dengue infections. Consistent with data reported in India, it was observed that a considerable number of patients diagnosed with DSS also had hyperbilirubinemia [24,27, 28]. Serum albumin concentrations are lower in these people than in non-dengue patients.

It was demonstrated that the albumin level and the severity of the illness were related, with the DF exhibiting the lowest albumin level found. DF's elevated vascular permeability and plasma leakage may be related to the observed drop in albumin levels. The reduction in blood albumin levels that was observed is similar to the results of other Indian studies [27, 28].

There was shown to be a relationship between renal impairment and the severity of the sickness. Higher levels of urea and creatinine were found in twenty per cent and sixty-two per cent of DSS patients, respectively, which served as evidence for this. The following findings of this study are consistent with those of earlier research [27,28,29]:

The lipid profile of DF was evaluated on days three, seven, and ten. The results showed that the levels of triglycerides and VLDL-c had risen. In contrast, the levels of total cholesterol, HDL-c, and LDL-c were lowered. There is a possibility that the decrease in levels of cholesterol, HDL-c, and LDL-c is due to the generation of cytokines and the interactions that these cytokines have with various aspects of lipid metabolism. This is because the cytokines that are generated by dengue, such as TNF and IL-1, interfere with the enzymatic mechanisms that are responsible for the formation of HDL and cholesterol, which results in a reduction in the production of these substances. An increase in the activity of a certain enzyme largely brings on higher triglyceride levels. This rise is brought about by an increase in the amount of lipolysis and de novo fatty acid synthesis that occurs in the liver. These two pathways are responsible for the elevated amounts of triglycerides that have been observed. Both the findings of the present inquiry and the conclusions that were reached from past studies [27, 28] were in agreement with one another. The levels of sodium, potassium, and calcium in the DF group were found to be considerably lower than those in the control group on the third, seventh, and tenth days of the experiment. Plasma leakage, which has been shown to be associated with severe dengue fever, might be the cause of this phenomenon. This investigation's results have been validated by previous research with similar findings. [29, 30].

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Conclusion:
Thrombocytopenia, leukopenia, and high hemoconcentration seem to be significant indicators of illness severity, according to the results given above. When tracking a patient's progress toward a full recovery, haematological indicators are crucial. It is possible to use the haematological profile as a screening tool to find out how the medication is working early on. Biochemical abnormalities such as elevated transaminase, urea, creatinine, and triglyceride levels and decreased albumin, sodium, potassium, calcium, cholesterol, HDL, and LDL levels can be used as indicators of dengue sequelae, as shown in this study. Extra care must be exercised while attending to patients whose criteria are compromised.

Conflict of interest:
The authors declare that they have no conflict of interest.

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