Prognosis of Dengue Fever based on Clinical Symptoms and Complete Blood Count in children aged 2-12 years

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ABSTRACT

Objective: We aim to investigate the value of Complete Blood Counts (CBCs) and clinical symptomatology of patients in determining the prognosis of dengue fever in children aged 2-12 years.

Study Design: Descriptive cross-sectional study.

Place and Duration: This study was conducted in Pediatric Department, HBS General Hospital Islamabad, over 3 months period, from 15th November 22, till 15th February 23.

Methodology: Patients who tested positive for either NS-1 antigen or dengue IgM antibody were enrolled in study. Demographic details of patients, clinical and hematological parameters, and daily progress of fever, serial CBCs and duration of hospital stay were recorded on a proforma. Data was analyzed using SPSS 22.00. Percentages of hematological and clinical parameters, average duration of fever and hospital stay were calculated.

Results: Dengue NS-1 antigen was positive in 94% of patients. Fever was seen in 88%, thrombocytopenia and leucopenia in 88% and 53% cases respectively. Thrombocytopenia and leucopenia improved within 5 days of admission in majority of patients. Average duration of improvement of symptoms and hospital stay was 3.5 days. A weak association between duration of hospital stay and lymphocyte count at admission was observed.

Conclusion: Dengue fever is a mild febrile illness in our study population. Thrombocytopenia was seen in majority of patients, yet none of them developed dengue hemorrhagic fever. Clinical symptomatology and complete blood count can act as monitoring tools in these patients. Majority of patients showed improvement in their clinical symptoms and hematological abnormalities within a week time and were discharged with follow up advised.

Keywords: Complete blood count, Dengue fever, Hematological abnormalities, Leucopenia, Prognosis, Thrombocytopenia.

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INTRODUCTION

Dengue fever is a syndrome characterized by biphasic fever, rash, arthralgia, myalgia, leucopenia and lymphadenopathy. It is caused by four types of dengue viruses (types 1, 2, 3 and 4) belonging to the family, Flaviviridae. These viruses are transmitted via a day time biting mosquito, Aedes Aegypti, which breeds in stored water and rain water.[1]

Dengue is highly endemic all over the world, with more than half of the world's population living in dengue endemic areas.[2] It is most common in tropical and sub-tropical areas of the world. In 2010, almost 390 million dengue infections occurred in the world.[3] Among Asian countries, dengue is highly endemic in Pakistan. According to Khan J et al, there have been 12 large outbreaks in Pakistan due to dengue fever resulting in 286,262 morbidities and 1,108 deaths. This study conducted in Peshawar district, showed 60% dengue cases with 21% cases of dengue hemorrhagic fever and 53.7% dengue shock syndrome.[4] It is common in all age groups, but 90% of dengue infections are seen in children less than 18 years of age.[5] Children also have 15 times higher risk of dying from secondary dengue infections as compared to adults.[6]

Clinical manifestations of dengue fever range from a mild acute febrile illness to dengue hemorrhagic fever (DHF) and dengue shock syndrome.[7] Dengue fever is characterized by fever, cough, rhinitis, retro-orbital pain, backache and sometimes a rash. Patients with dengue hemorrhagic fever (DHF) have cold extremities, warm trunk, decreased urine output, restlessness and irritability. There may be petechiae, bruises and ecchymoses. Approximately 20-30% of these patients go on to develop dengue shock syndrome (DSS). Respirations are rapid, pulses are weak and liver is enlarged.[1]

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Positive reverse transcriptase polymerase chain reaction (RT-PCR) assay during the first five days of illness along with detection of viral antigen non-structural protein 1 during first seven days of illness are considered standard for diagnosis.[8] Serological tests (IgG or IgM based) are used to diagnose dengue infection after a few days of infection. IgM antibodies are produced after 5 days of symptom onset and may persist for 2-3 months. First time dengue infections have a higher IgM antibody response, while secondary infections have a higher IgG antibody response. The Standard Diagnostic IgG based ELISA has a sensitivity of 81.2% and specificity of 39.8%.[9] Hematological changes seen during infection are leucopenia, thrombocytopenia and hemoconcentration. Thrombocytopenia is a predictor of dengue hemorrhagic fever. It is seen in about 50% cases of dengue fever and almost 100% cases of dengue hemorrhagic fever.[10] Hemoconcentration is seen due to plasma fluid leakage in dengue hemorrhagic fever. Identification of early indicators of prognosis is vital to decrease the fatality rate associated with dengue fever.[11]

In this study, we aimed to establish the value of complete blood count in determining the prognosis of dengue fever in children. In resource poor settings where advanced prognostic indicators cannot be employed due to financial constraints and lack of infrastructure, complete blood count is most commonly used test to decide admission and discharge of patients. It can act as an early indicator of prognosis in dengue patients based on initiation and recovery trend of platelet and white blood cell count. Symptomatology of Dengue fever ranges from mild illness to dengue shock syndrome. By observing the disease pattern in our patients, we can devise guidelines for management of dengue fever in our target population. This will help in reducing the disease burden in health care facilities especially in resource poor settings.

METHODOLOGY

This was a descriptive cross-sectional study conducted over three months, from 15th November 2022 till 15th February 2023. It was conducted in Paediatric in-patient Department in HBS General Hospital Islamabad. Study was started after taking consent from ethical review committee of HBS Medical and Dental College Islamabad (EC, 12/11/2022). Non-probability consecutive sampling was done. Patients aged 2-12 years, who tested positive for non-structural protein 1 (NS-1) or dengue immunoglobulin M (IgM) antibody were included in study. Exclusion criteria was patients who had pancytopenia secondary to other causes, hematological disorders, chronic liver disease and who were on immunosuppressive drugs such as steroids. Exclusion was done on the basis of history, examination and previous investigation record.

Leucopenia was defined as White blood cells < 4000/mm^3 and thrombocytopenia < 150,000/mm^3. Discharge criteria was improvement in pattern of fever and recovery trend of platelet count. Prognosis of disease was defined as length of hospital stay, duration of fever and that of hematological abnormalities on complete blood count.

The demographic details of patients, their presenting complaints, duration of hospital stay was recorded on a preformed proforma. Details of laboratory investigations were entered that included total leucocyte count, differential leucocyte count, platelet count, and hematocrit and laboratory diagnosis of dengue fever. Average three CBCs were performed for each patient, with at-least one at admission and discharge each. The frequency of tests was decided by clinicians based on their clinical judgment. Patients were discharged when their fever and platelet count started to improve.

Data analysis: It was performed on SPSS version 22.00. Demographic and clinical data were presented as descriptive statistics. Frequency and Percentages were calculated for gender, clinical features, and hematological derangements such as leucopenia, thrombocytopenia and dengue confirmatory tests (NS-1 antigen and serology). Average duration of hospital stay was calculated. The pattern of recovery of platelets and WBCs was studied on different days. Correlation coefficient and p-Value was calculated between length of hospital stay and percentage of neutrophils and lymphocytes. A p-Value of less than 0.05 was considered statistically significant.

RESULTS

Total 34 patients were included in this study, out of which 22 were male (65%) and 12 (35%) were female. Average age of patients was 7.7 years and duration of hospital stay was 3.41 ± 1.28. Among the clinical features, fever was the most common symptom seen in 88% of cases, backache in almost 40 %, headache and vomiting in 30% and pain abdomen in 6%.

Diagnostic tests for confirmation of disease were carried out which showed Dengue NS-1 antigen positivity in 94% of patients and dengue IgM antibody in 6% of patients. Hematological abnormalities on complete blood count showed that 88% of our patients developed low platelet count < 150,000. While, leucopenia was seen in 53% of the patients.

Table I: Duration of Fever (N=34)

Duration of fever (number of days)	Frequency n (%)
1	0
2	12 (35.2%)
3	6 (17.6%)
4	10 (29.4%)
5	4 (11.7%)
6	0
7	0
8	0
9	2 (6%)

Table I shows duration of fever in different patients. Patients remained febrile for 2 to 9 days, with an average duration of fever of 3.5 days.

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Table II: Duration of Hospital Stay (N=34)

Duration of hospital stay Number of days	Frequency n(%)
1	2 (5.8%)
2	8 (23.5%)
3	8 (23.5%)
4	8 (23.5%)
5	6 (17.6%)
6	0
7	2 (5.8%)

Table II shows the duration of hospital stay in days in dengue patients. Duration of hospital stay ranged from one to seven days with an average duration of 3.5 days.

Table III: Initiation and Improvement of Thrombocytopenia and Leucopenia (N=34)

Thrombocytopenia & Leucopenia	Day 1 n (%)	Day 2 n (%)	Day 3 n (%)	Day 4 n (%)	Day 5 n (%)
Thrombocytopenia Initiated	24 (70.5%)	4 (11.7%)	2 (6%)	-	-
Leucopenia initiated	8 (23.5%)	8 (23.5%)	2 (6%)	-	-
Thrombocytopenia Improved	-	8 (23.5%)	12 (35%)	6 (18%)	4 (11.7%)
Leucopenia Improved	-	4 (11.7%)	4 (11.7%)	8 (23.5%)	2 (6%)

Table III shows that thrombocytopenia developed in our patients in initial 3 days of hospital admission. While, both thrombocytopenia and leucopenia improved by fifth day of illness

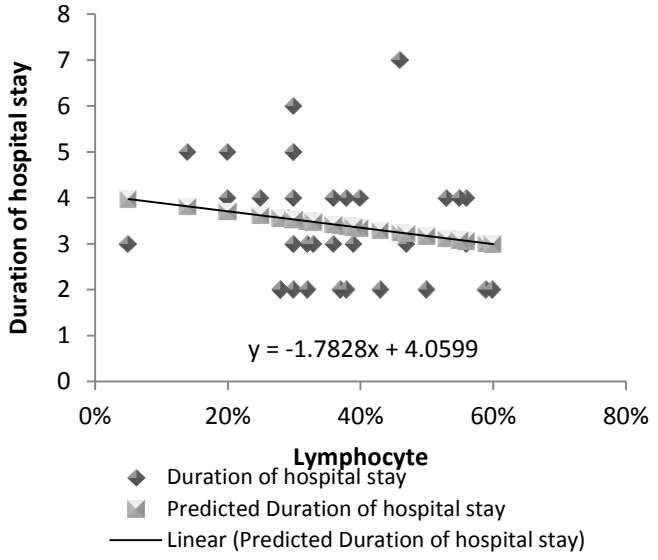

Figure 1: Association of lymphocyte percentage in differential leucocyte count with duration of hospital stay

Figure 1 shows association of lymphocyte percentage with duration of hospital stay at the time of admission using regression with line-fit plot. There is a reduction in hospital stay as lymphocyte percentage increases. Correlation coefficient was calculated between lymphocyte count and hospital stay showing value of r = 0.18 which shows weak relationship between lymphocyte count and hospital stay with a p-Value = 0.31 which is insignificant.

DISCUSSION

Dengue fever is an important re-emerging Arboviral disease in tropical and sub-tropical regions of the world including Southeast Asia.[12] Pakistan is one of the 125 dengue endemic countries of the world. Multiple factors are responsible for this high incidence of dengue fever in Pakistan such as change in climate, virus evolution and social factors such as increasing urbanization, higher population growth and world-wide travel and trade. Dengue fever is found to be more common in younger than in the older age group.[13] Especially, severe dengue is considered to occur in infants and children in South America, Southeast Asia and other countries.[14]

The mean age of our study group was 7.7 years. In a study conducted in a secondary care hospital in Islamabad, Pakistan, the mean age of patients was also found to be 7.9 ± 2.8 years.[15] The proportion of male patients (65%) was found to be almost double than the females (35%) which was consistent with the results of other studies also. Khetpal et al also found 61% male patients with dengue fever and 39% females.[16] Possible reasons for this sex related difference can be use of fully covered dresses by female children and prioritizing provisions of male children in society.[17] However, in a study by Tchuandom et al, more females were affected by dengue fever (7.7%) than male children (4.7%).[18] Female predominance (54.8%) was also seen in study by Farooq et al.[15] Common clinical manifestations of dengue fever are fever, backache, vomiting, abdominal pain, petechiae. In our patients, fever was the most common symptom seen in 88% of patients. Khetpal et al also found fever to be the most common symptom seen in 100% of their study cases.[16] It was followed by lethargy, myalgias, abdominal pain and vomiting. Most of our patients were diagnosed on the basis of NS-1 antigen that was positive in 94% of cases and IgM antibodies in 6% of cases. These results were very similar to that seen in a study conducted in Bangladesh that showed NS-1 antigen to be positive in 94.2% of cases and IgM antibody in 5.8% of cases[15]. Average duration of fever in our patients was 3.5 days while it was found to be 5 days by Khan et al in their study.[17]

Further in this study, we determined the percentage of patients who developed thrombocytopenia and leucopenia that was found to be 88% and 53% respectively. Khan et al also found in their study a higher percentage of thrombocytopenia (87.2%) and leucopenia (40.4%).[19] Both these laboratory abnormalities can result from bone marrow suppression in patients with dengue fever. Thrombocytopenia is considered a marker for monitoring the severity of dengue fever as established by WHO and supported further by various research studies.[20,21] Our research showed thrombocytopenia in majority of patients but it improved in less than a week duration showing a non-severe form of the disease. None of the children went on to develop dengue hemorrhagic fever. A study conducted by Sachdev et al

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found that abnormalities of platelet and WBC count had inconsistent association with dengue severity.[22] In a study by Ananda Rao et al, lymphocytosis had a negative correlation with hospital stay of patients. Children who had lymphocytosis on initial differential cell count had a shorter length of hospital stay.[11] In our study, a weak association between duration of hospital stay and lymphocytosis at admission was found showing a shorter duration of hospital stay with increased lymphocyte count.

Despite the high prevalence of dengue fever in Pakistan, there is still lesser data on characteristics and clinical outcomes of children hospitalized with dengue fever. A local study conducted in National Institute of Health, Karachi, also found a promising outcome of children admitted with dengue fever with no mortalities and fewer complications like disseminated intravascular coagulation and pleural effusion in their study population.[5]

CONCLUSION

Dengue fever is a mild febrile illness in our study population. Thrombocytopenia was seen in majority of patients, yet none of them developed dengue hemorrhagic fever. Clinical symptomatology and complete blood count can act as monitoring tools in these patients. Majority of patients showed improvement in their clinical symptoms and hematological abnormalities within a week time and were discharged with follow up advised.

Recommendation

Patients of dengue fever with deranged hematological parameters can be managed on outdoor basis with close follow up. This will help in reducing the hospital burden in resource deficient settings.

Limitations of Study

This was a single-centered study performed over three-month period, resulting in a small sample size. The interval between consecutive CBCs was not consistent in all patients as it was based on clinician's discretion.

AUTHOR'S CONTRIBUTION

Qayyum H: Manuscript writing, Conception and design.
Rabia M: Final approval of version, Revising the work critically
Sohail S: Revising the work critically. Analysis of data
Zafar T: Acquisition and interpretation of data.

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