An Evaluation of Haematological Changes in Paediatric Dengue Fever Patients at a Tertiary Care Hospital Rawalpindi during 2019 Outbreak

Rai Muhammad Asghar¹, Rai Rijjal Ashraf², Khalid Saheel³, Abid Hussain⁴

¹ Professor, Department of Paediatrics, Benazir Bhutto Hospital, Rawalpindi.
² Medical Officer, Department of Paediatrics, Benazir Bhutto Hospital, Rawalpindi.
³ Assistant Professor, Department of Paediatrics, Benazir Bhutto Hospital, Rawalpindi.
⁴ Senior Medical Officer, Department of Paediatrics, Benazir Bhutto Hospital, Rawalpindi.

Author’s Contribution

Paper Type: Original Article

Abstract

Objective: The study aimed to evaluate the hematological parameters of patients with dengue fever in order to increase the sensitivity of screening for early diagnosis and as an aid to the early institution of appropriate treatment.

Materials and Methods: This study was conducted in Pediatrics Department Benazir Bhutto Hospital, Rawalpindi for a period of 6 months from July 2019 to December 2019.

Results: During the study period of 6 months, 438 dengue serology-positive children were admitted, amongst which 254 were male (58%), and 184 were female (42%). The children’s age ranged from 1 month to 12 years, with a mean age of 8.03 years (SD ± 3.13 years). Out of 438 children, 254 (58%) were uncomplicated dengue fever (DF), 119 children (27%) developed dengue hemorrhagic fever (DHF). 65 children (15%) went into dengue shock syndrome (DSS). The predominant findings in the complete blood picture (CBC) were Thrombocytopenia (80.1%) and leucopenia (65.1%). Normal leucocyte count was seen in 59 cases (13.68%). Thrombocytopenia (platelets less than 100,000) was seen in 351 patients (80.1%) out of which 30 cases (6.9%) had a platelet count less than 50,000. Leukopenia was found in 285 (65.1%) patients. Most of the patients were positive for NS1 (70.3%). IgM was positive in 62.1% and IgG was positive in 14.8%. Enteric Fever as co-infection was found in 30(6.8%) children.

Conclusion: Careful assessment and interpretation of hematological changes in dengue patients allow early diagnosis and institution of appropriate treatment.

Keywords: Dengue, platelets, children.
Introduction

Dengue is a public health concern as it is a global life-threatening infection. In more than 100 countries it affects about 2.5 billion people. Dengue is transmitted by mosquitoes and leads to arthropod-born viral diseases. Dengue virus is a member of the Flaviviridae family and has four different antigenic types (dengue 1, 2, 3 & 4). The principal vector is Aedes aegypti which bites during the daytime.

The main presenting features are fever, headache, myalgia, arthralgia, and minor haemorrhagic manifestations. A wide range of manifestations can occur in infection with any of the dengue virus infections and vary from mild fever to haemorrhage and shock which is life-threatening. Correct and early diagnosis can help improve patient management and optimized the use of resources such as hospital staff, beds, and equipment.

The laboratory test for dengue is of two types, Non-specific tests like complete blood count and definitive tests like dengue serology and NS1 antigen test. The epidemiological aspects of the disease, the kit, and the method used may result in variations in these tests results.

During the disease process, a series of haematological and biochemical changes occur which depend upon the clinical disease.

The clinical features of dengue infection may resemble other infections. The serological tests are expensive and are not available in many hospitals. Awareness of clinical features, as well as laboratory findings like haematological and biochemical parameters, are the most important guides to therapy and prognosis of dengue fever. The haematological and biochemical findings reported are thrombocytopenia, anemia, leukopenia, elevated levels of AST & ALT. Other findings are activated lymphocytes on a peripheral blood smear. Lymphocytosis and neutrophilia and raised bilirubin can also occur. Changes in haematocrit, albumin, and cholesterol can also occur. Other changes are hemoconcentration, a raised blood urea and serum creatinine, hypokalemia, DIC hypocalcemia. The study aimed to evaluate the haematological parameters of patients with dengue fever to increase the sensitivity of screening for early diagnosis and as an aid to the early institution of appropriate treatment.

Materials and Methods

This prospective descriptive study was conducted at the Department of Pediatrics, Benazir Bhutto Hospital, Rawalpindi for a period of 6 months from July to December 2019. One month to 12 years old children presenting with clinical signs and symptoms of dengue fever were admitted to the paediatric dengue ward and were included in the study. Patients with age more than 12 years or suffering from previously known blood disorders were excluded. All children attending the hospital with symptoms and signs suggestive of dengue fever were tested for NS1 antigen and IgM/IgG dengue antibody serology (depending on the day of fever) by enzyme-linked immunosorbent assay (ELISA) technique. Every admitted case with confirmed dengue fever was enrolled in a structured protocol that included relevant hematological investigations. The diagnosis of dengue fever was based on the WHO criteria. All this data was recorded and entered in the predesigned, pre-tested, and semi-structured questionnaire. The relevant data was recorded, entered, and analyzed by SPSS version 24 for descriptive statistics and bivariate analysis.

Results

During the study period of 6 months, 438 confirmed dengue patients were admitted, amongst which 254 were male (58%), and 184 were female (42%). The age of the children ranged from 04 months to 12 years, with a mean age of 8.03 years (SD + 3.13 years).

Table 1: Demographic and Clinical Presentations

| Gender | Frequency (n=438) | Percentage |
|--------|------------------|------------|
| Male   | 254              | 58         |
| Female | 184              | 42         |

| Age (mean 8.03 years SD ± 3.13) | Frequency |
|-------------------------------|-----------|
| Less than 1 year              | 15        |
| 1-4 years                     | 78        |
| 5-8 years                     | 114       |
| 9-12 years                    | 231       |

In our study, out of 438 children, 254 (58%) were reported as uncomplicated dengue fever, 119 children (27%) developed dengue hemorrhagic fever and were managed accordingly. 65 children (15%) were into dengue shock syndrome and treated for this complication.
In our study, the main findings were thrombocytopenia (80.1%) and leucopenia (65.1%). Leucocyte count was normal in only 59 patients (13.68%). 351 (80.1%) patients had Thrombocytopenia (platelets less than 100,000). 94 (21.7%) patients were positive for NS1 (70.3%). IgM was positive in 62.1% and IgG was positive in 14.8%. Enteric fever as a cop infection was seen in 30 patients, ALT was deranged in 42% of patients, and AST was elevated in 27.85%.

Table 3: Laboratory Findings.

| LABORATORY HEMATOLOGICAL FEATURES | Mean (± SD) | Minimum | Maximum |
|-----------------------------------|------------|---------|---------|
| Total Leukocytes Count            | 4.5 x 10³  (± 2.5) | 1.1 x 10³ | 18.6 x 10³ |
| Hemoglobin                        | 11.59 (± 2.32) | 4.9 mg/dl | 16.9 |
| Platelets                         | 82.6 x 10³ (± 48.1) | 9 x 10³ | 351 x 10³ |
| Hematocrit                        | 33.84% (± 5.59) | 18.9% | 52.7% |

Thrombocytopenia, Leukopenia, HCT > 20% with Platelets <50,000, deranged LFTs, Hyponatremia, Hepato-spleenomegaly, and Gall bladder wall thickness on Ultrasonography were seen significantly associated with Progression of Disease and Development of Complications.

Table 4: Significant Laboratory Parameters for Development of Complications

| SIGNIFICANT LABORATORY PARAMETERS FOR DEVELOPMENT OF COMPLICATIONS | Variable | DF N=254 | DF N=119 | DF N=65 | P-Value |
|------------------------------------------------------------------|----------|----------|----------|----------|---------|
| TLC                                                              | <4,000   | 165      | 77       | 43       | 0.991   |
| (Mean 4.5x10³ ± 2.5 SD)                                          | 4,000 – 10,000 | 83     | 37       | 20       |         |
| >10000                                                           | 06       | 05       | 02       |          |         |
| Platelets                                                       | >100,000 | 56       | 07       | 04       | 0.001   |
| (Mean 82.6 ± 48.1 SD)                                           | 50,000 – 100,000 | 95     | 102      | 48       |         |
| <50,000                                                         | 03       | 10       | 17       |          |         |
| HCT                                                             | >35      | 249      | 101      | 57       | 0.002   |
| (33.84% ± 5.59 SD)                                              | <35      | 05       | 18       | 08       |         |
| ALT                                                             | <100     | 234      | 89       | 40       | 0.000   |
| (Mean 104 ± 55 SD)                                              | 100 - 1000 | 20     | 29       | 21       |         |
| >10000                                                          | 00       | 01       | 04       |          |         |
| AST                                                             | <100     | 234      | 89       | 40       | 0.000   |
| (Mean 262 ± 295 SD)                                             | 100 - 1000 | 20     | 29       | 21       |         |
| >10000                                                          | 00       | 01       | 04       |          |         |
Discussion

Dengue infections are asymptomatic in 75% of infected humans. A spectrum of disease, from self-limiting dengue fever to haemorrhage and shock may be seen. A complex interaction of host and viral factors occur and determine whether the infection will be asymptomatic, typical, or severe. CBC parameters such as hemoglobin (Hb), hematocrit (Hct), WBC count, differential percentages of WBCs, and platelet count alter each day of fever in patients infected with dengue. Pancytopenia may develop after 3-4 days of illness. Early and accurate laboratory diagnosis of dengue virus infection is critical to effective patient management.

Amongst the age and sex ratio, the majority of the children are in the age group of 8-12 years, boys more commonly affected than girls with male to female ratio of 1.2:1. A similar age group with a mean age (standard deviation) of 6.9±3.3 years and a higher male to female ratio of 1.2:1 was found in a study by Potha pregada S et al. A study by Manoj Kumar et al. also shows a higher number of males affected with a male to female ratio of 1.54:1 among all seropositive cases.

The most significant laboratory abnormality seen in our study was thrombocytopenia. A study has shown thrombocytopenia in 59.8%. Another study has found thrombocytopenia in 67% of the cases. Significant derangements in platelets were found in yet another study. A study by Adel Hamed has documented thrombocytopenia in 74.45% of the patients. As platelet counts decrease the complication rate increase and duration of hospital stay increase with decreasing platelet count. Platelet count can therefore be used to predict the complication and duration of hospital stay and hence better use of resources.

In our study concomitant presence of leucopenia, raised haematocrit and low platelet count were commonly associated with dengue fever with warning signs. Leucopenia and differences in WBC count in dengue fever & dengue haemorrhagic fever have been found in a study by Juthatip Chaloemwong et al., demonstrating leucopenia (WBC count<5000 cells/mm) in 70.9% of the patients during the acute febrile phase (day 2, 3) of illness with the average value in the acute febrile phase of 4.38 and 4.49 in those who progressed to dengue haemorrhagic fever. Other studies have documented leucopenia in 66% of patients and 26.5% of patients.

In our study liver enzymes were in the range of 10 - 3500, with three children having a value of more than 3000. ALT& AST levels were significantly increased among severe dengue cases compared to uncomplicated dengue fever cases. An elevation in AST (45.1%) and ALT (17.6%) were found in a study by Ferede et al. Kularatnam et al. has found that AST and ALT levels begin to rise in the early febrile phase with the median concentration of AST of 746 u/L and ALT median concentration of 118 u/L. In our study, hemoglobin levels varied between 4.9 mg/dl and 16.9 mg/dl with a mean of 11.59 mg/dl (±2.32), while hematocrit varied between 18.9% and 52.7% with a mean of 33.84 (±5.59).

Conclusion

Careful assessment and interpretation of hematological changes in pediatric dengue patients not only allow early diagnosis but also aid in adopting appropriate treatment.

References

1. Hasan S, Jamdar SF, Alalowi M et al. Dengue Virus: A global human threat: Review of literature. J Int Soc Prev Community Dent. 2016 Jan-Feb; 6(1):1-6.
2. Schaefer TJ, Panda PK, Walford RW. Dengue Fever[updated 2020 Apr 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan.
3. Halstead SB. Dengue Fever, Dengue Hemorrhagic Fever and Severe Dengue. In: Kligrman R M, St Gme III JW, Blum NJ, Shah SS, Tasker RC, Wilson KM, Behrman RE (edit). Nelson Textbook of Pediatrics: 21st Ed. Philadelphia PA:Elsevier 2020; 1760-1764.
4. Clinical Features and Laboratory findings of Dengue Fever in German Travelers: A Single-Centre Retrospective analysis
5. Muller DA, Depelsenaire ACI, Young PR. Clinical and Laboratory Diagnosis of Dengue Virus Infection. J Infect Dis. 2017 Mar; 215(2):S89-S95.
6. Phukkaiwonkong K, Chaovalit P, Jittamala P, Blacksell SD, Carter MJ, Turner P, et al. Predicting the severity of dengue fever in children on admission based on clinical features and laboratory indicators: application of classification tree analysis. BMC pediatrics. 2018 Dec; 18(1):1-9.
7. Chan HBY, How CH, Ng CWM. Definitive tests for dengue fever: when and which should I use? Singapore Med J. 2017 Nov; 58(11):632-635.
8. Raafat N, Blacksell SD, Maude RJ. A review of dengue diagnostics and implications for surveillance and control. Trans R Soc Trop Med Hyg. 2019 Nov; 113(11):653-660.
9. Kularatnam GA, Jasinge E, Gunasena S, Samarannayake D, Senanayake MP, Wickramasinghe VP. Evaluation of biochemical and haematological changes in dengue fever and dengue hemorrhagic fever in Sri Lankan children: a prospective follow up study. BMC pediatrics. 2019 Dec 1; 19(1):87.
10. Mane V, Mohite S. Clinicopathological study of 50 cases of dengue fever. Int J Med Rev 2015; 3(8):794-799.
11. Gitika, Grag M, Gill GS. Evaluation of Hematological and Biochemical Profile of Early Dengue. Int J Contemp. Med Res. 2018;5(6):F1-F4.
12. Mannimuth VG, Balla S, Kumar KJ. Serum ionic calcium levels and hypocalcemia in dengue fever in children and its correlation with its severity: case control study. Int J Contemp Pediatr. 2019 May; 6(3):1289-1293.
13. Jain D, Rajput R, Pathak V, Mittal A, Jain P. Changing Trends in Clinical Presentation and Biochemical Spectrum of Dengue Fever: An Observation of a Tertiary Care Centre. Archives of Clinical Infectious Diseases. 2017 Jul 31;12(3).
14. Pothapregada S, Kamalakannan B, Thulasingham M, Sampath S. Clinically profiling pediatric patients with dengue. Journal of global infectious diseases. 2016 Jul;8(3):115.
15. Kumar M, Verma RK, Mishra B. Prevalence of Dengue Fever in Western Uttar-Pradesh, India: A Gender-Based Study. Int J Appl Basic Med Res. 2020 Jan-Mar; 10(1):8-11.
16. Tewari K, Tewari VV, Mehta R. Clinical and Hematological Profile of Patients with Dengue Fever at a Tertiary Care Hospital – An Observational Study. Mediterr J Hematol Infect Dis. 2018 Mar 1; 10(1):e2018021.
17. Deshwal R, Qureshi M I, Singh R. Clinical and Laboratory Profile of Dengue Fever. J Assoc Physicians India. 2015 Dec; 63(12):30-32.
18. Abdulhamed MH. Hematological changes in children with dengue fever in Saudi Arabia. Egypt J Haematol. 2017; 42(4):129-133.
19. Jayanthi HK, Tulasi SK. Correlation study between platelet count, leucocyte count, nonhemorrhagic complication and duration of hospital stay. J Family Med Prim Care. 2016 Mar; 5(1):120-123.
20. Ralapanawa U, Alawattegama AT, Gunrathne M, Tennakoon S, Kularatne SA, Jayalath T. Value of peripheral blood count for dengue severity prediction. BMC research notes. 2018 Dec;11(1):1-6.