Pattern of Haematological and Biochemical Parameters of Dengue Virus Infection in Children

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Abstract

Objective: This study was conducted to study pattern of clinical, hematological and biochemical parameters in children with dengue fever.

Method: A prospective comparative analysis of 120 suspected febrile children was done at social security teaching hospital in Lahore from September to November 2021. The study participants satisfying the inclusion criteria were registered for further assessment. Clinical findings were logged, hematological and biochemical parameters tests were performed.

Results: In this study, there were 56.66 % male participants and 43.33 % female participants. The most common clinical manifestation was fever (100%) followed by vomiting 85.4%, abdominal pain 68.75% and body pain / myalgia in 52.08% cases. Most frequent hematological parameter was thrombocytopenia (93.75%) followed by leucopenia 70.83% and the elevated levels of liver transaminases were seen in 68.75% subjects.

Conclusion: This study focuses on the patterns of laboratory parameters of pediatric dengue viral infections .This might prove helpful for the pediatricians to suspect, diagnose and manage the dengue virus infection.

Key Words: Dengue virus infection, Dengue fever, Dengue hemorrhagic fever, Hematological tests, Biochemical parameters.

Introduction

Dengue is an Arbo viral disease which is transmitted by mosquito.[1] The Aedes aegypti is the culprit for its transmission. Dengue infection has rapidly spread across the globe in the recent decades.[2] The seasonal transmission is mainly seen in monsoon and post monsoon time of year.[3,4]

According to the estimation of WHO, this world's two third population is at the risk of the dengue virus infection, particularly the tropical and subtropical countries[1]. While dengue is endemic in many countries, majority cases are reported from Southeast Asia and the western Pacific regions.[3] In South East Asian region, India is one of the seven countries that has reported high incidence of dengue outbreaks threatening the health care system badly[4]. In 1940's, India reported firs confirmed case of dengue fever & after that more states started reporting this.[5,6] In Bangladesh its true magnitude was essentially unknown until it manifested heavily in 2000.[4,7]

In Pakistan, first outbreak of DHF was confirmed in Karachi that happened in 1994 with total 145 cases and only one case of fatality was reported.[8] Punjab has now encountered this infection for more than a decade and is passing on to hyperendemicity.[1,2]

Dengue infection has demonstrated great variations in presentation from mild illness to complicated dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[7,9] As compared to adults, the severity of this

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disease (DHF) is seen more in children belonging to the age group of under 15 years.[10,11] There are four discrete serotypes of dengue virus which are DENV 01, DENV 02, DENV 03 and DENV 04. Lifelong immunity is acquired only if the infection happens to be with one serotype of dengue virus (DENV), because the protection provided against the subsequent infection is partial and transient.[12] For the effective management of dengue outbreaks, the knowledge of exact clinical presentation, epidemiology and laboratory profile is of utmost importance. Since long time, several studies are being carried out to observe the trends in the epidemiological pattern of dengue transmission through geographical mapping of severe dengue fever cases, which has enabled to predict future outbreaks and to focus the system of public health.[13,14]

In clinical practice, Dengue virus infection is primarily diagnosed with the help of clinical presentations and laboratory data. There are some non-specific tests; e.g. hematological parameters, liver function tests, and serum protein concentration and few specific tests; such as viral antigen test and serology for antibody detection used to aid in diagnosis.[9,13,14]

Attempts must also be made to identify additional factors for early diagnosis of the disease severity and swift supportive treatment of infected patients. Specific treatment for dengue is not available, but early disease identification and appropriate fluid replacement therapy, use of antipyretics and analgesics along with quality nursing care certifies the decline in the mortality risk due to severe cases.[15]

It is crucial to comprehend the risks of developing dengue outbreaks as well as the biochemical picture of this disease in order to have proper utilization of the resources.[9,15] In the post-monsoon season, we usually get a resurgence of this infection. Hence, a hospital-based study in children was conducted, in order to determine the trends in laboratory parameters of DF & DHF. This study highlights the biochemical characteristics of dengue fever and might be helpful for future management of disease more effectively.

Material and Methods

The study involved 120 suspected cases of Dengue fever and were followed prospectively at Social Security Hospital, Multan road Lahore in the department of Pediatric Medicine. It was a simple comparative study. This was done during the dengue outbreak occurring between the months of September to November 2021. Patients were selected through convenient purposive sampling technique. These 120 patients of age group 1-15 years which were labelled as suspected, probable and confirmed dengue as per Dengue GCP guidelines. Confirmed dengue patients were then further classified as dengue fever, dengue hemorrhagic fever (grade I –IV) according to Dengue GCP guidelines.

A predesigned patient proforma with all details of epidemiology, clinical and laboratory parameters was used as a tool for data collection during the hospital stay, Clinical examinations was performed by a doctor on each study participants and all details were noted in the structured questionnaire.

Hematological profiles and biochemical investigations were done at the time of admission and were followed by daily (or bi-daily) investigations as per need. All of these parameters on day five were mainly assessed and used for comparison in this study.

All the routine investigations such as hematological determiners like total leukocyte count (TLC), differential leukocyte count, platelet count; hemoglobin (Hb) and hematocrit (Hct) were checked by the automated blood analyzer. Transaminases levels for liver function tests and total serum protein were done by the automated biochemistry analyzer. The cutoff values of each test results were considered based on reference ranges used by the laboratory.

Signs of plasma leakage were monitored by CXR and abdominal USG. Specific investigations were also done in some patients as required to avoid confusion with similar epidemic febrile illnesses, like cerebrospinal fluid analysis, neuroimaging, viral markers, peripheral smear and serology for plasmodium falciparum, blood culture and sensitivity. All the categorical variables such as clinical features and biochemical parameters were expressed as numbers and percentages. The predominant laboratory features in each group were documented and analysed for their statistical significance

Statistical analysis was performed by Chi Square test done by using the Statistical Package for Social Sciences (SPSS 15.0) .Comparison of two groups was assessed by applying t-test ,with $p < 0.05$ considered as statistically significant. The study protocol was approved by the Ethics and Research Committee of social security teaching hospital and a written informed consent was obtained from the parents or guardians.

Result

Out of 120 enrolled suspected dengue cases 68 (56.66%)

were male while 52 (43.33%)were female. Majority of the confirmed dengue patients were male 29 (60.41%) and 19 (39.58%)of the patients were female. The most dominant age group among the suspected and confirmed dengue patients was >10-15 yrs. Out of these 120 suspected Dengue cases, 90 (75 %) were labeled as probable dengue but 48 (40%) were later confirmed to have dengue infection. Of the confirmed dengue fever patients, 32(66.66%) patients had classic dengue fever while 16(33.33%) fulfilled the criteria of dengue hemorrhagic fever (DHF). Of these 16 patients with dengue hemorrhagic fever, 25% (12)patients were of DHF grade I/II, 8.33% (4) patients were of DHF grade III and none with DHF grade I (Figure 1).

Thrombocytopenia (platelet count < 150,000/mm^3) was the most common hematological finding observed in 45(93.75%) cases, followed by leucopenia (TLC < 4,000/mm^3) seen in 44 (91.66%) cases. Platelet count of >100,000 /mm^3 to <150,000/ mm3 was seen in 15 (31.25%) cases while count below 100,000 / mm^3 in 30 cases. All the patient falling in group of DHF had platelets count of <100,000/mm^3. Anemia (Hb < 11.0 g/dl) was seen in 25 (52.08%) children. Hematocrit > 50 % was observed in 22 (45.83 %) of the cases. Neutrophil count of < 1500 in 5 (10.41%) and lymphocyte count of > 3000 in 3(6.25 %) cases was observed (Table 1).

The study of the biochemical investigations depicted that alanine aminotransferase (ALT) level > 45 IU/L (85±7 IU/L)was present in 28 (58.33 %) of cases and aspartate aminotransferase (AST) level > 35 IU/L (97 ± 9 IU/L)was observed in 31(64.58%) of cases. Hypoproteinemia (4.8±0.7 g/dl) was observed in 11 (22.91 %) cases. Deranged PT/APTT were found in 13 cases (27.08%) (Table 2). Serositis in the form of ascites and pleural effusion in 20 (41.66%) cases. Pericholecystic edema was found in 10 (20.83%) cases(Table 2).

On comparison of laboratory parameters, thrombocytopenia of less than 100,000/mm^3 was observed in 43.75% cases with DF but in all patients with DHF. HCT >50% was found in all patients with DHF but in 18.75% of patients with DF . 68.75 % cases with DHF showed prolonged PT/APTT in contrast to only 6.25 % of cases with DF that was statistically significant. Both groups showed rise in transaminases with no statistical difference. Hypoalbuminemia was observed in 9 out of 16 (56.25%) cases with DHF and only 2/32 (6.25%) patients with DF (Table 3 & Figure 2).
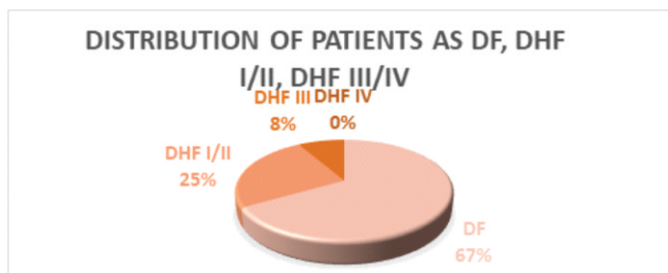

Figure No 1: *Distribution of patients as DF, DHF I/II, DHF III/IV (DSS).*

Table 1: *Hematological Profile Of Dengue Cases:*

| Parameter	No. of Patients (n=48)	Percentage (%)
HEMOGLOBIN		
< 11 g/ dl (9.5 ±0.7g/dl)	25	52.08%
>11 g/dl (11.2 ±0.6g/dl)	23	47.91%
Hematocrit (%)		
>50% (54±2 %)	22	45.83%
TLC		
<4000 cell/cumm (2800 ± 500 cell/mm^3)	34	70.83%
>4000 cell/cumm (4800 ± 600 cell/mm^3)	14	29.16%
NEUTROPHILS		
>1500 cell/mm^3	43	89.58%
<1500 cell/mm^3	5	10.41%
LYMPHOCYTES		
>3000 cell/mm^3	3	6.25%
<3000 cell/mm^3	45	93.75%
PLATELETS		
>100,000-<150,000 cell/mm^3 (120,000 ±10,000 cell/mm^3)	15	31.25%
<100,000 cell/mm^3 (55,000 ± 20,000 cell/mm^3)	30	62.5%
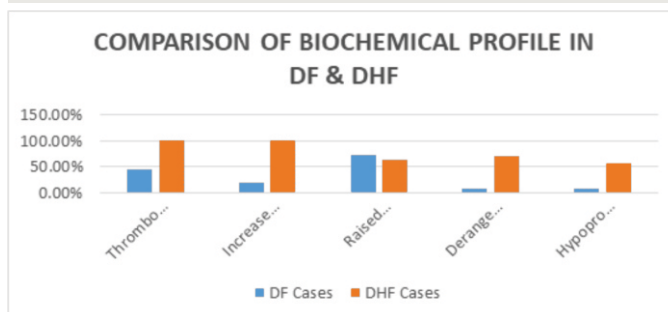
Figure No 2: *Comparison of Biochemical Profile in DF & DHF:*

Table 2: *Biochemical & Radiological Profile Of Dengue Cases:*

Parameter (± SD)	No. of Cases (n=48)	Percentage (%)
ALT >45 IU/L (85±7 IU/L)	28	58.33%
AST > 35 IU/L (97 ±9 IU/L)	31	64.58%
SERUM PROTEIN <5.5 g/dl (4.8±0.7 g/dl)	11	22.91%
PT/APTT ABNORMAL	13	27.08%
PLEURAL EFFUSION / ABDOMINOPELVIC ASCITES	20	41.66%
PERICHOLECYSTIC EDEMA	10	20.83%

Table 3: *Comparison Of Biochemical Profile In DF & DHF:*

Parameter	Confirmed Cases (n= 48)	DF	DHF	P Value
Thrombocytopenia <100,000cell/mm^3	30 (62.5%)	14 (43.75%)	16 (100%)	<0.05*
HCT >50%	22 (45.83%)	6 (18.75%)	16 (100%)	<0.05*
Raised Transaminases	33 (68.75%)	23 (71.87%)	10 (62.50%)	>0.05
Deranged PT/APTT	13 (27.08%)	2 (6.25%)	11 (68.75%)	<0.05*
Hypoproteinemia	11 (22.91%)	2 (6.25%)	9 (56.25%)	<0.05*

*P value of < 0.05 is considered to be significant.

Discussion

In past few years, the prevalence of dengue has increased globally. Therefore timely diagnosis and appropriate medical management are of prime importance.

This study has emphasized on patterns in hematological and biochemical profile of children with dengue infection. The evidence hence generated is crucial for better understanding of management of children presenting with dengue infection. Dengue fever shows laboratory alterations beginning on the third day and getting most evident on the 5th day and restoring to normal usually by the eleventh day.[13,14,15]

The most frequent finding was thrombocytopenia (platelet count < 150,000/mm^3), observed in 45(93.75%) cases. Thrombocytopenia might be related to decreased platelets production due to viral bone marrow suppression, or due to binding of dengue antigens to platelets and increased antibody mediated immunological platelets destruction. Tejas found thrombocytopenia to be 92.68 % while studying the trends in biochemical profile of dengue patients.[20] A study by Jayant also found thrombocytopenia to be the consistent finding as it was observed in 84% cases of classical dengue and 100% cases of dengue hemorrhagic fever.[17] Similar was found in Srilankan study by Jayadas.[18] Payal Jain reported a significant proportion of patients (80%) with platelet count below 100,000/cumm and 41.2% with platelet count below 50,000/cumm.[19]

Leucopenia is another hematological parameter which occurs in dengue infected patients due to dengue bone marrow suppression. This study found leucopenia (TLC < 4,000/mm^3) in 44 (91.66%) cases. This is in contrast to study by Ferede et al in which leucopenia was observed in 26.5% of the cases20. Tejas showed it to be 58.26%[16].

Jayadas from Sri Lanka observed leukopenia in 85% of the NS1 positive patients.[18]

Anemia (Hb < 11.0 g/dl) was seen in 25 (52.08%) children in our study. Ferede et al found Hemoglobin levels less than the cutoff values in 44.1% of the cases[20]. This could be explained due to mucosal bleed.

Hematocrit > 50 % was observed in 22 (45.83%) of the cases, which is related to the hemoconcentration due to increased intravascular plasma permeability, the basic pathophysiological mechanism in dengue infection. Increased hematocrit was observed in 6.9% cases by Ferede et al.[20]

Dengue virus is hepatotrophic and also cause damage to other organs; hence leading to excess release of AST (nonhepatic source like erythrocytes, brain & kidney tissue, skeletal & cardiac and muscle) during infection and ALT associated with hepatocytes injury that leads to more deranged AST than ALT. Elevated transaminases were seen in 33 children comprising 68.75% in our study group. AST was raised in 64.58% and ALT in 58.33% of our cases. Ferede et al also observed higher of AST in 45.1% and ALT in 17.6% of the cases with AST being in a greater proportion than ALT.[20] This observed pattern might be explained on the basis of excess AST release from damaged muscle cells (nonhepatic source) during infection leading to more derangement in AST than ALT. Payal Jain also documented mild to moderate elevation in the levels of AST and ALT in 85.1% and 80.7% of the patients, respectively.[19] In a study of Sri Lanka, Jayadas showed the raised aspartate transaminase (AST) levels in 63 (80.7%) patients and

elevated alanine transaminase (ALT) level was found in 32 (52.5%) patients.[18] Tejas documented raised liver enzymes in 79.94%[16].

In our study, hypoproteinemia (total protein < 5.5 mg/dl) was observed in 11(22.91 %) cases. In studies by Ferede et al documented hypoproteinemia in 30.77% cases.[20] This could be probable that the complex interaction between virus, host immune response and endothelial cells, may affect the barrier integrity and vascular endothelial cells functioning leading to plasma leakage and hypoproteinemia. Our study revealed deranged PT/APTT in 13 cases (27.08%). Altered coagulation profile was observed in 37% patients in study by Jayant[17]. This abnormality in the coagulation profile is explainable on the basis of hepatotrophic effect of dengue virus.

Our study revealed serositis in 20(41.66%) cases. Contrary to this, Payal Jain's study showed the radiological evidence of serositis in 16.67% cases.[19] Our study showed pericholecystic edema in 10 (20.83%) cases. Tejas studied found it in 48.23% cases.[20]

Conclusion

The community infection of dengue virus is characterized by the ice berg phenomenon. The knowledge of pattern of hematological and biochemical profile will help the clinician in early diagnosis and effective management of the patients with dengue fever. More studies regarding this in pediatric age group will prove fruitful.

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Authors Contribution

SS: Conceptualization of Project

KMA: Data Collection

SS, MA: Literature Search

MAF: Statistical Analysis

KMA: Drafting, Revision

SSC, ME: Writing of Manuscript