Original Article

Dengue Fever

Evaluation of Predictors for Severity of Dengue Fever at the Beginning of the Disease

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ABSTRACT

Objective: To evaluate the predictors of severity of dengue at the beginning of the disease

Study Design: Prospective and Observational study

Place and Duration of study: This study was conducted at Shan General Hospital and Trauma and General Hospital from July 2010 to 1st October 2011.

Patients and Methods: The study was conducted on all patients who were admitted and confirmed to have dengue fever after positive serology on day VI. There was pre-assigned protocol and every predictive marker was given one point.

Results: Patients who had ≥ 4 points at the time of presentation had more severe illness and developed more severe complications rather than those who had ≤ 2 points.

Conclusion: Dengue fever is becoming a major health problem. Predictive markers for severity of illness may help in detection of complication and its management.

Key Words: Dengue fever, Dengue hemorrhagic fever, Dengue shock syndrome, predictive markers

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INTRODUCTION

Dengue is one of the most prevalent mosquito borne infection, which recently has become a major international public health burden. It is approximated that over 100 million dengue virus infections happen each year throughout the world.[1] Dengue is a major hazard in tropical and sub-tropical regions around the world, mostly in urban and sub-urban areas. Dengue haemorrhagic fever (DHF), was first recognized in 1940's during the dengue epidemics in Phillipines and Thailand, as a fatal threat, but today DHF affects most Asian countries.[2] It belongs to members of the family Flaviviridae, genus flavivirus.[3] There are four nearly related, although serologically distinct viruses known as DEN-1, DEN-2, DEN3 and DEN-4.[4]

The clinical demonstration of dengue viruses varies from asymptomatic, self limited dengue fever to DHF associated with shock syndrome. The severity of illness increases in sequential rather than primary infection.[5]

An starling rise of dengue virus with complications is increasing in our part of the world in recent years.[6] We undertook this study in two different hospitals of Karachi from different locations. We elaborated selected patients, presenting with signs and symptoms of dengue fever and were followed up as per pre-assigned study protocol.

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PATIENTS AND METHODS

This prospective and observational study was conducted at Shan General Hospital and Trauma and General Hospital during the period of July 2010 to 1st October 2011. Predictors for severity of illness were designed prior to the commencement of study. They were designed according to the clinical features and laboratory parameters of the illness. Every predictor was given 1 point. The predictors for severity of illness included: ALT>50 IU, APTT >3sec from control, WBC <3000 on arrival, platelets <150,000 on arrival and fever of high grade with severe back pain. Patients having ≤ 2 points at the time of presentation had less chances of receiving platelets during the course of illness due to thrombocytopenia. Around 30% of patients require platelet transfusion. Patients with >3 points had 45% chances of receiving platelet transfusion and patients >4 points had 80-100% chance of requiring platelets infusion and they also had chances to develop DHF. Total 120 patients were included in the study from both hospitals, sixty from each hospital, with suspected history and clinical features of dengue fever. Out of 120 patients 90 were males. The age range among male patients was 18 ± 7 years and among females it was 30 ± 7 years. All patients admitted

undergone complete blood count, erythrocyte sedimentation rate, malarial parasite, liver function test, prothrombin time (PT), activated partial thromboplastin time (APTT), urea, creatinine, and electrolytes at the time of admission and were repeated on days III, VI and X. At the time of admission they also had blood C/S, urine detailed report, urine C/S, ultrasound abdomen and chest X-ray. Dengue serology was sent on day VI of onset of symptoms.

Inclusion criteria: Patients with positive IgM or IgM and IgG both for dengue virus.

Exclusion criteria: Individuals with pre existing liver disease secondary to hepatitis B or C, patients with autoimmune illness and those who were on anticoagulants for any reason.

Patients with classical features of dengue but had negative dengue serology on day VI, were excluded from the study.

RESULTS

Patients with severe form of illness at the time of presentation i.e. having more than two symptoms and signs and having decreased platelet count (< 100,000).

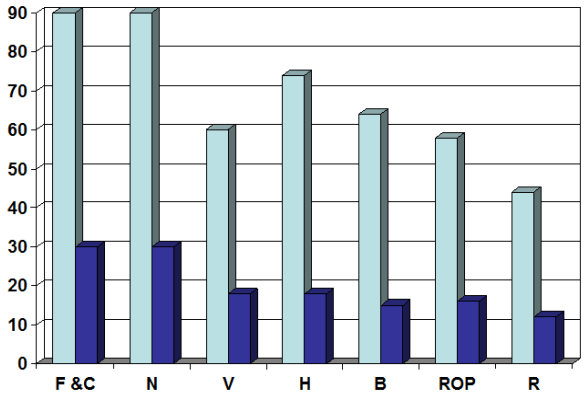
Regarding symptoms of dengue fever, among 120 patients more than 50% had 3 symptoms at the time of presentation (figure 1).

Bleeding is one of the main features of dengue fever which also predicts the severity most. Precisely in our 120 patients, 6 had bleeding from multiple site and rest of the patients had it from one site (figure: 2).

On examination patients revealed different presentation (figure. 3).

Every patient had certain laboratory test on day one and then on subsequent days. The average of that result is shown in table 2 and 3.

Patients having platelet count less than 50,000 had twice daily platelet count.

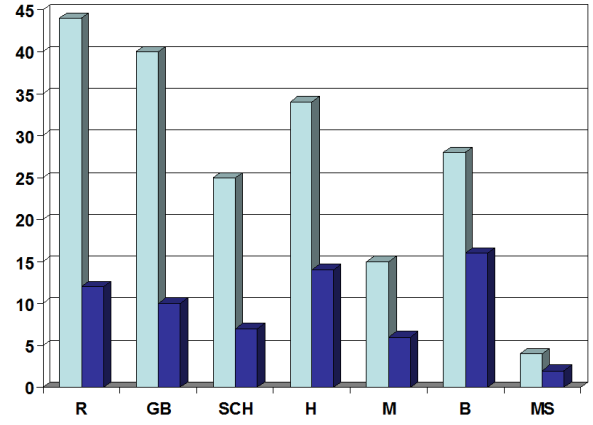


F & C: Fever and chills, **N:** Nausea
B: Vomiting, **H:** Headache, **B:** Bodyache,
ROP: Retro-orbital pain, **R:** Rash

Figure No. 1: Different symptomatology at the time of presentation Male = 90, Female = 30

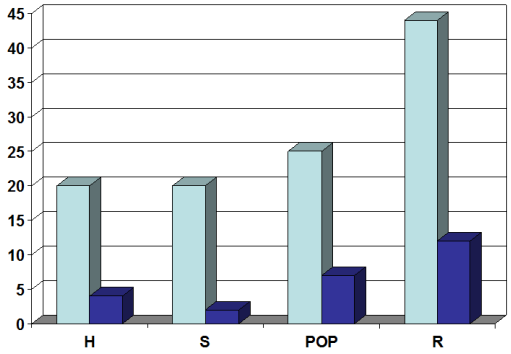
In our study total 7 patients had ≥ 4 points at the time of presentation. Eighteen patients had ≥ 3 points and 95 had ≥ 2 points at presentation (table 4).

Patients having ≥ 4 points at the time presentation have severe disease, or patients requiring platelet transfusion for multiple times had the increase chances of developing severe form of dengue fever i.e. DHF or DSS.



R: Rash **GB:** Gum Bleeding
SCH: Sub Conjunctival Haemorrhage
H: Haematuria **M:** Malena
B: Bruises **MS:** Bleeding from multiple sites

Figure No. 2: Different bleeding pattern of the patients Male=90, Female=30



H: Hepatomegaly **S:** Splenomegaly
POP: Peri orbital puffiness **R:** Rash

Figure No. 3: Different signs during illness Male=90, Female=30

Table No.1: Pre assigned predictive laboratory parameters on different days to evaluate the severity

	Day 1	Day 3	Day 6	Day 10	Day 12
WBC Count	<4,000	<2.500	<1.500	>3.500	>4000
Platelet Count	<150,000	<100,000	<50,000	> 100,000	>150,000
APTT	3-6 sec	7-9 sec	>9 sec	< 3 sec	3 sec
ALT	70	200	400	< 70	<45
Crea-tinine	1.4	1.6	>1.6	1.2	1.0

Table No.2: Laboratory parameters among male patients n=90

	Day 1	Day 3	Day 6	Day 10	Day12
WBC Count	86	86	81	81	88
Platelet Count	86	88	49	81	84
APTT	62	36	12	78	90
ALT	75	40	22	74	90
Creatinine	12	6	4	84	90

Table No.3: Laboratory parameters among female patients n=30

	Day1	Day 3	Day 6	Day 10	Day12
WBC Count	26	18	9	22	28
Platelet Count	24	16	14	21	26
APTT	15	5	3	7	30
ALT	18	9	5	21	30
Creatinine	6	4	2	20	30

Table No.4: Points achieved by patients on arrival to the hospital n=120

Points	Total patients	SGH	TGH
≥ 4	7	4	3
≥ 3	18	10	8
≥ 2	95	48	47

DISCUSSION

Dengue is a pyretic illness that is caused by flavivirus and is endemic in more than 100 countries in tropical and sub tropical countries.[7] It is seen that mild dengue disease contributes more than half of the total public health burden of dengue associated illness, [8] the more grave manifestations of DHF and DSS provide the major impact for effects to prevent infection.[8,9] Dengue virus transmissions follow two general pattern, either epidemic or hyper endemic. Epidemic dengue transmissions occur when the introduction of dengue virus into a region is an abandoned event involving one virus strain.[10] Epidemicity is right now the predominant pattern of dengue virus transmission in smaller island nations, certain areas of South Africa and Asia. Hyper endemic transmission elaborates the continuous circulation of multiple dengue virus serotypes in the same area. Areas with hyper endemic dengue virus transmission contribute the vast majority of cases of dengue virus infection throughout the world. Between 5-10% of the susceptible population experience dengue virus infection annually in same region.[11,12] South East Asia extending from southern China to Southern Taiwan included in the hyper endemic area, as A aegypti is present throughout the region. Pakistan and India experienced major out breaks of dengue fever in 2007, hyper endemic circulation of all four dengue serotypes appear to be established.[13] Majority of dengue virus infections produce mild, non specific symptoms or classic dengue fever. The more severe manifestations DHF and DSS, accounts only for less than 1% of infection, which is also seen in our observation. Only 5% of our patients develop severe dengue fever and complications of dengue virus fever. The low risk of serious illness leads to the attention towards understanding the risk factor as well as to look for predictive marker for severity.

The risk factor includes type 2 genotype which is more prevalent in our part of the world.[14,15] Prior dengue exposure is another risk factor and it is also seen in our patients as those who had second episode of dengue develops more severe illness. It is also proven in other studies as one study from Bangkok[16]and one from Myanmar[17] proven the same result. The risk of dengue decline with age, especially after age 11, as we did not compare our adult patients with children so this is not observed in our study. Unlike other infectious disease dengue is more common is well nourished population rather than malnourished. This may be due to suppression of cellular immunity in malnutrition.[18]

The clinical features of dengue fever vary in different age groups. Infants and young children may present with nonspecific febrile illness with rash. Older children and adults either manifest as a mild febrile syndrome or the classical disease with sudden onset and high grade fever, severe headache, pain behind the eyes, muscle and joint pain with or without rash. All these symptoms were manifested by our patients. Because dramatic plasma leakage can develop suddenly and usually after a few days of fever, consequential attention has been advised upon the early identification of patients at higher risk for shock and other complications. Leukopenia, thrombocytopenia and a haemorrhagic diathesis are the characteristic haematologic findings in dengue virus infection. Leukopenia is one of the earliest presentation of the illness, and is of similar degree in DHF and dengue fever.[19] Thrombocytopenia is common in both dengue fever and DHF, but marked thrombocytopenia $<100{,}000/mm^3$ is one of the criteria to define DHF. Multiple factors are responsible for fall in platelet count and are most severe late in the illness.[20] Manifestation of haemorrhagic diathesis in dengue virus infection range from a positive tourniquet test to life threatening haemorrhage. Mild elevation of serum aminotransferases is common in both dengue haemorrhagic fever, and it is noted earlier in illness. Deranged coagulation profile (PT, APTT) is another predictor for severity of illness.[21] In our study we have seen that patients coming with low leukocyte, low platelets, increase AST and deranged coagulation profile earlier the disease have more severe illness rather than those with near normal levels at the beginning of illness.

CONCLUSION

It is concluded that dengue fever is a common public problem which is increasing every day, but DHF and

DSS are still not the main issue. Appropriate investigation, strict monitoring and appropriate supportive treatment can reduce the mortality in dengue fever. Predictive markers can reduce the mortality if used promptly. Thus it is advisable to use the predictive markers for the early detection of complications and then appropriate management.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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