Clinical Manifestations and Laboratory Profile of Dengue Fever among the Patient's General Hospital, Penang

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Abstract

Objective: The aim of this study was to evaluate the clinical presentation of dengue fever among the patients admitted to the Public Hospital Pulau Penang, Malaysia.

Materials and Methods: A cross-sectional study was planned to attain the objective of this study. Retrospective analysis of the records was conducted, all the confirmed cases registered from Jan 2007 till Dec 2007 were the part of study. Data collection was conducted using a structured data collection form cover the information about the demographic, clinical presentation, lab features and management of patients.

Results: A total of N=756 cases were the part of study; myalgia was the frequently observed 148 (57.6%) symptom for the dengue hemorrhagic fever (DHF), followed by hepatomegally 50 (19.5%) and in cardiac complications myocarditis was observed 4 (1.6%) in DHF cases. While bleeding from gums (16.7%), epigastric pain 5 (83.3%), ascites and pleural effusion 1 (16.7%) were the clinical features observed in Dengue Shock Syndrome (DSS). Lab investigations have showed that Hess test was found positive for 88 (34.2%) patients diagnosed with DHF.

Conclusion: Conclusion DF, DHF and DSS should be considered in a differential diagnosis of febrile illness in patient's, DHF and DSS are complications of dengue which is required early identification in association with thoroughly monitoring and basic supportive care to save the life of the patients. It is compulsory to monitor strictly thrombocytopenia, haemo-concentration and liver profile on routine basis.

Keywords

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Introduction

Dengue is an acute illness caused by *Aedes* mosquito, commonly caused by *Aedes* aegypti and *Aedes* albopictus. It is an endemic disease in South East Asian countries especially in Malaysia. Over population, rural–urban migration, weak public health infrastructure and highly growth of consumerism favorable conditions for mosquito vector, *Aedes* aegypti growth and transmission of viral transmission to human subjects [1].

Malaysia is located in the tropics; Dengue is a major problem for its people. Dengue Fever (DF) was first reported in 1902 in Penang State [2] and had become a major public health problem in Malaysia. As Dengue Hemorrhagic Fever DHF outbreak was appeared in Penang in 1962 [3], notification of DF and DHF in Malaysia was reported in 1971. The incidence rate of clinically diagnosed DF and DHF reported had increased from 8.5 cases/100,000 populations in 1998 to 123.4 cases/100,000 population in 1998. In the year 2001, 16,368 cases were reported, of whom 22% were among children 14 years and below. In the year 2001, the DH: DHF ratio in children was 6.7:1 in adults [4]. In Penang despite of the presence of the range of disease since 1902 no documented evidence exists that provide some current evidence on the prevalence of dengue fever, therefore it is necessary to investigate their clinical features on disease severity base and laboratory findings to improve its diagnosis and management.

Materials and Methods

This was cross- sectional study conducted at a tertiary care hospital i.e Public Hospital Pulau Penang. Retrospective evaluation of records was done; all the registered patients with confirmed diagnosis of DHF, from Jan-2007 till Dec- 2007 were the part of study.

Ethical Consideration

The study protocol was approved by Clinical Research Committee (CRC) of the hospital.

Data collection

Patient's records were reviewed and the data was collected using a structured data collection form that covers the information about the demographic, clinical presentation, lab features and management of patients. The management protocol was included regular clinical and laboratory assessments of bleeding tendencies and haemo- concentration, monitoring of vital parameters.

Statistical analysis

A non-parametric statistics was applied, x^2 statistics was applied to explore the association among the variables. However, in the case where the expected cell count was less than 5, Fisher exact test was preferred over x^2 statistics. Further, t-test was applied to find out the differences in the laboratory parameters at two different times for the same subjects. P-value <0.05 was considered statistically significant.

Results

Of the total 756 dengue patients were diagnosed 493 (65.2%) of DF, 257 (34.0%) DHF and 6 (0.79%) were as DSS patients. All the cases were confirmed by IgM ELISA. In this study the clinical characteristics were investigated on the basis of disease severity (DF, DHF and DSS) in patients with confirmed dengue virus infection, all the cases with dengue virus infections confirmed by any of the diagnostic tests were categorized as DF, DHF and DSS according to WHO criteria. The results are enumerated in Table 1.

Table 1: Clinical features according to disease severity dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

Clinical features	DF N (%)	DHF N (%)	DSS N (%)	P-value	Total N (%)
Fever	493(100%)	257(100%)	6(100%)	-	-
Arthralgia	199 (40.4%)	130(50.6%)	2 (33.3%)	0.021*	331 (43.8%)
Myalgia	233 (47.3%)	148(57.6%)	3 (50.0%)	0.021*	384 (50.8%)
Hess test	75 (15.2%)	88 (34.2%)	2 (33.3%)	<0.001*	165(21.8%)
Island of white in the sea of red	17 (3.4%)	11 (4.3%)	0 (.0%)		28 (3.7%)
Macular papular rashes	28 (5.7%)	27 (10.5%)	1 (16.7%)	0.022*	56 (7.4%)
Petechial rash	32 (6.5%)	32 (12.5%)	2 (33.3%)		66 (8.7%)
Gum bleeding	40 (8.1%)	42 (16.3%)	1 (16.7%)		83 (11.0%)
Epistaxis	31 (6.3%)	20 (7.8%)	1 (16.7%)	0.004*	52 (6.9%)
GIT(Hematmesis / melaena)	0 (.0%)	1 (.4%)	1 (16.7%)		2 (.3%)
Epigastric pain	186 (37.7%)	118(45.9%)	5 (83.3%)	0.023*	309 (40.9%)
Ascites	0 (.0%)	12 (4.7%)	1 (16.7%)	<0.001*	13 (1.7%)
Pleural effusion	1(.2%)	23 (8.9%)	1 (16.7%)	<0.001*	25 (3.3%)
Encephalitis (convulsions)	1(.2%)	6 (2.3%)	0 (.0%)	0.037*	7 (.9%)
Myocarditis	1(.2%)	4 (1.6%)	0 (.0%)	<0.001*	5 (.7%)
Total (DF,DHF,DSS)	493	257	6	-	-

Fisher exact test, p-value significant <0.05

Discussion

Dengue characteristics according to disease severity, DF, DHF, DSS

In the present study the patients were classified according to the criteria of WHO into DF, DHF and DSS [1]. Clinical manifestations were studied on severity grades of the disease in all the admitted patients of dengue. Of the total 756 dengue cases were diagnosed as 493 (65.2%) DF cases, 257 (34.0%) DHF, 6 (0.79%) of DSS. All the cases were confirmed by IgM ELISA tests. Fever was the most common presenting symptom 100% in all of the patients. In other studies fever was observed in most of the DF patients [5]. Arthralgia and mayalgia, general skin rashes, island of white in the sea of red, erythematous rashes, macular popular rashes and petechial rashes were highly associated with dengue fever.

The arthralgia and myalgia nearly equally were present in the DF, DHF and DSS and found statistically significant (P=0.021). Presence of myalagia, flushing, macular popular rashes or scattered petechia was the most predictive features of dengue fever as other non dengue diseases [6]. Island of white in the sea of red, macular popular rashes and petechial rashes were also noted in DHF comparatively less to DF and were statistically significant (P=0.022). While in DSS cases, island of white in the sea of red was absent, macular popular rashes and petechial rashes were present to lower extent. It was reported in a study that the presence of petechiae significantly related to minimum number of platelets [7].

The Hess test or tourniquet test is a simple clinically test procedure that reflects capillary fragility and has been reported that to be positive in nearly all of the DHF cases [8].

Table 2: Laboratory measures at the time of admission and discharge in the hospitalized patients

Parameters	Units	N	Mean value of WBC	SD	Change in (%)	P-value
WBC at the time of admission	10^3/uL	756	3.98	2.68		
					29.90	<0.001*
WBC at the time of discharge			5.71	3.31		
HCT at the time of admission	%	756	40.93	5.90		
					-2.96	<0.001*
HCT at the time of discharge			39.69	7.26		
Plt at the time of admission			76.58	62.66		
	10^3/uL	756			18.36	<0.001*
Plt at the time of discharge			90.64	64.30		
Alanine transaminase at the time of admission			84.20	196.30		
	u/L	756			-24.89	<0.001*
Alanine transaminase at the time of discharge			63.33	119.4		

Paired t-test, p-value significant <0.05

In the present study Hess test was found 15.2% in DF and 34.2% in DHF but was observed high in DHF and only 33.3% present in DSS. The results were statistically significant (P<0.001). In the previous studies found that in majority of the DHF patients had positive Hess test and has yielded a positive results in children and has been considered as a screening test for dengue infection in the WHO severity classification [1,9]. In many Asian countries tourniquet test has been reported in many studies in a study conducted by Qui *et al.*, 1993 in which the tourniquet test 66.9% [10] was positive and by Halstead studied the clinical features of dengue in Thailand and reported 81 % cases were positive for tourniquet test, while in Puerto Rico it was found 32 - 31% which is different from the study conducted in Thailand [11]. Therefore, it had been mentioned in the earlier study that tourniquet test with the presence of flushed face used as a enrolment criteria for that study had sensitivity 90%,a specificity of 97% as a positive predictive value of 97% for diagnosis of dengue virus infection [12]. Therefore, the physicians should take it in notice about this small predictive value to distinguish dengue fever and hemorrhagic cases.

In this study bleeding from gums, epistaxis and from GIT in DF was noted 8.1%, in DHF 16.3% and in DSS 16.7%, epistaxis in DF was found 6.3%, in DHF 7.8%, 16.7% in DSS. Bleeding from GIT was low in our study and was observed 0.4% in DHF and 16.7% in DSS and found significant (P=0.004). The causes of the bleeding could be due to thrombocytopenia, consumption coagulopathy, capillary fragility or platelet dysfunction, as thrombocytopenia was a continuous finding, no correlation established between the platelet counts and bleeding manifestations indicating that other features such as a disturbance in platelet function and capillary fragility contribute to the bleeding diathesis [13]. In other studies the bleeding tendencies had found in DF 9% and in DHF 18% which is greater than DF compared to DHF [14]. A study conducted in China the common hemorrhagic manifestations were generally lower the epistaxis and gum bleeding at

multiple sites or at different occasion [10]. Bleeding was studied from various sites and was found 72% gum bleeding and epistaxis were the common bleeding manifestations 40% [13].

Epigastric pain was found in DF cases 37.7%, in DHF was found 45.9% and 83.3% in DSS and found statistically significant (P=0.023). Epigastric pain which was common in all grades of dengue infection but was minimum in DF and frequently found in DHF and DSS patients, which indicates that epigastric pain associated with severity of the disease. In another study similar findings were reported in DF 28% and in DHF 41% [14]. It was found in all grades of disease, therefore it is a limited symptom to give a diagnostic value of disease severity.

In the present study the ascites was only found 4.7% in DHF cases and in DSS was present 16.7 % and was statistically significant (P<0.001). In our study ascites and pleural effusion were diagnosed on clinical basis and chest radiograph examination revealed the presence of ascites and pleural effusion. In a study conducted during out break in Delhi 1996, 5.5% ascites were examined in DHF and DSS patients [15]. Pleural effusion in our study was found in all grades of disease and was found statistically significant (P<0.001) and found positive association with disease severity. However was higher significantly 16.1% in DSS cases. Pleural effusion in a study conducted during out break in Delhi 1996 8.2% were detected in DHF cases [15]. Pleural effusion or ascites detected by chest x-rays in DHF patients with no clinical evidence of these findings has been reported earlier in pediatric patients with DF [16]. Encephalitis (convulsions) was found statistically significant (P=0.037) in DF and DHF cases, however was observed higher in DHF patients compared to DF. According to the findings found in a study in Jakarta by Sumarmo *et al* ., 1983, in 33% of the patients were

reported convulsions [17]. According to many other studies neurological dysfunctions have been reported in DHF, (Kalayanarooj *et al.*, 2002). In a study reported by Nimmannitya *et al.*, 1987 only one-fifth of the 24 children with neurological manifestations were in shock, while children with DSS may have abnormal neurology secondary to cerebral hypo perfusion on account of shock leading to hypoxic ischemic events or intracranial bleeds (Nimmannitya *et al.*, 1987). In a study it was shown that in some cases breakdown of the blood brain barrier in the CNS may occur (Ramose *et al.*, 1998). Other important reasons for neurologic manifestations include cerebral edema, direct neutrotropic effect of dengue virus resulting encephalitis (Lum *et al.*, 1996).

Myocarditis is a complicated clinical symptom of dengue fever and was found in our study in 5 (0.7%) patients. In DF 0.2% while in DHF 1.6% was found and was statistically significant (P<0.001). Similar findings were also found in a descriptive study conducted in Sri Lanka, 5 cases were there of myocarditis. In these five patients myocarditis led to hypotension and circulatory failure in five patients. They all recovered except one. This may be due to misinterpreted as DSS and excess fluid may have given developing fatal acute heart failure (Kularatne *et al.*, 2005).

Laboratory parameters at the time of admission and discharge

In our study total of 756 patients were evaluated. We examined the laboratory features of dengue patients admitted to the hospital. Clinically relevant laboratory parameters were defined by normal laboratory ranges for each variable. White blood cell count was counted at the time of admission and at discharge time. The average mean was at admission time 3.98×10^3/uL and at discharge was found 5.71×10^3/uL which is significantly higher than was at the time of admission (P<0.001) and the difference in percentage 29.90% was found. White blood cell count which shows a predictive value of dengue fever. In a study this parameter has been predicted to have positive predictive value for dengue in similar studied on children and adults presenting with febrile illness in Thailand [14,15].White blood cell counts had strong association with dengue fever.

Haematocrit concentration was evaluated the mean found at admission time 40.9% and was statistically highly significance (P<0.001). It reveals a very good association with dengue fever and calculated the percentage difference from admission to discharge 2.96%. Thrombocytopenia (low platelets count) was seen in our study; at the time of admission the mean average was noted 76.58×10^3/uL, while at the time of discharge it was come up to 90.64×10^3/uL, the significant difference was found (P<0.001) and the mean percentage difference was found 18.36% which increased in the platelets count at the time of discharge. In our findings white blood cells count examined strongly associated with dengue fever, hematocrit and platelets were also significantly associated with dengue fever. The laboratory finding white cells count was found lower at the time of admission and is one of the sign for indication of dengue fever. This feature of WBC had been shown to have a positive predictive value for dengue fever in similar studies conducted on children and adults presenting

with febrile illness in Thailand [15]. Hematocrit in the studies of Thailand indicated that the mortality from DHF occurs as a result of hypovolaemic shock which is in turn; resulted from increased capillary permeability leading to raised haematocrit [1]. Therefore, WHO has included raised haematocrit as one of the important criteria for DHF. Haemoconcentration may be due to low value of hemoglobin or due to chronic anemia.

Thrombocytopenia was evaluated in the present study and the platelets were significantly associated with dengue fever and commonly considered as one of the diagnostic feature of the disease. A sever thrombocytopenia of less than 50,000 per cubic millimeter was found in 74% of fatal cases in Thailand [17].

In another study it was reported that 94% of the 977 patients with DHF had platelet counts 82% had less than $100,000m^3$ [18]. It is mandatory to monitor strictly thrombocytopenia and haemoconcenteration on routine basis. Similar studies were conducted in which they have evaluated WBC count, hemoglobin, hematocrit and thrombocytopenia [19]. In a study conducted by Kittigul and colleagues, 300 suspected cases of dengue were diagnosed by screening clinical criteria, fever with positive tourniquet test and leucopenia or, thrombocytopenia or haemoconcenteration in which 286 cases (95.3%) were serologically confirmed as having dengue virus.

In our study the laboratory parameter was observed alanine transaminase to be lower in dengue patients than the reference ranges. Alanine transaminase was found with the mean of 84.20U/L at the time of admission which was higher than the normal ranges and upon discharge alanine transaminase was observed 63.33 U/L and was statistically significant (P<0.001) and the percentage difference from the time of admission to the time of discharge was noted to 24.89 %. Alanine transaminase in the present study was observed a good indicator for dengue infection. Liver is affected by dengue infection. Alterations in liver enzymes of AST and ALT were found and elevation in serum AST appears to be greater than ALT levels. In another study performed in Mexico the mean value of aspartate AST and alanine aminotransferase ALT were 212 IU/L and 169 IU/L respectively [20]. On the basis of the findings of this study liver was affected by dengue infection.

Conclusion

DF, DHF and DSS should be considered in a differential diagnosis of febrile illness in patient's, DHF and DSS are complications of dengue which is required early identification in association with thoroughly monitoring and basic supportive care to save the life of the patients. It is compulsory to monitor strictly thrombocytopenia, haemoconcentration and liver profile on routine basis.

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