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EVALUATION OF CLINICAL FEATURES AND COMPLICATIONS OF DENGUE-INFECTED PATIENTS IN PENANG GENERAL HOSPITAL, MALAYSIA

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ABSTRACT

The purpose of the study was to observe the clinical features and complications of dengue infection. Admitted patients to the medical ward with dengue virus infection were studied in the General Hospital Penang, Malaysia. A total of 756 patients were enrolled from January 2007 to December 2007. The clinical features were evaluated and compared in terms of age groups. The patients were distributed in four different age groups. Children ≤18 years, young age groups 19 to 36 years, adults 37 to 54 years and the elderly age group ≥55 years old. The differences in clinical features between children and adults require further evaluation to identify and recognise the substantial factors involved. Ascites, jaundice, and pleural effusion are the complications of dengue, which require early identification in association with thorough monitoring and basic medical support to save the lives of dengue patients.

INTRODUCTION

Today, dengue is a fast-growing health problem in tropical and sub-tropical countries. The definition of dengue fever is stated as "an acute illness caused by a virus belonging to the family Flavivirus, under the genus Flavivirus". Dengue is the most common disease among all arthropod-borne viral infections in the world today. There are four serotypes of dengue virus, namely Den-1, Den-2, Den-3, and Den-4, which exist in an urban transmission cycle in tropical and sub-tropical areas by the Aedes aegypti (WHO, 1997). Infection with one serotype develops long-lasting immunity against re-infection by that same serotype, but not against the other serotype.

MATERIALS AND METHODS

A retrospective study was conducted on the admitted patients in the hospital in Penang during the period January 2007 to December 2007. There were 756 patients studied, from which data were collected from the charts and records of admitted patients General Hospital Penang. Information about the patients was recorded on the standard form.

ETHICAL CONSIDERATION

The study was approved by the Clinical Research Committee (CRC) Penang GH, reference number 2008/05.

SELECTION CRITERIA OF THE STUDY POPULATION

It consists of the following two criteria.

INCLUSION CRITERIA

1) Patients were considered for the study with a confirmed diagnosis, complete records of dengue fever from January 2007 to December 2007.

2) All inpatients were included in the study.

EXCLUSION CRITERIA

1) Missing or incomplete data (record) was excluded.

2) Patients with complicated cases, like surgical cases, cancer, and HIV, were excluded

The clinical features of dengue fever in patients were mentioned in terms of age groups. And were divided into four groups. Children were considered less than 18 years or equal, 19-36 young age groups, from 37-54 years adults and ≥55 years old. The patients with dengue infection were diagnosed by the WHO, 1997 criteria.

Statistically, the features were tested by applying the Fisher exact test to determine the clinical features in terms of age.

RESULTS

Fever was defined as the fever before admission and during hospitalisation. Fever was present in all 756 admitted patients. Arthralgia and myalgia were observed among children 43 (20.3%) and 53 (25.0%), respectively. While in the young age groups (19 –36 years), arthralgia and myalgia were common and were found in 160 (52.5%) and 195 (63.9%), respectively. In the aged 37 – 54 years old patients arthralgia and myalgia were found prominently, 104 (65.5%) and 110 (59.8%) respectively. While the lowest level was seen in the age of 55 years and above, 24 (43.6%) and 26 (47.3%) respectively, the (P <.001) found statistically significant. The rashes were evaluated in different age groups, with islands of white in the sea of red; macular popular rashes were present to a mild level in the age group 18 years and below 4 (1.9%), 12(5.7%), respectively. On the other side, in the age group of 19 – 36 years, occurred 8 (2.6%), 28 (9.2%), 22 (12.0%), 43 (14.1%), 30 (9.8%) respectively. These features also occurred in the age group of 37 – 54 years, 11 (6.0%), 12 (6.5%), 9 (4.9%), 22 (12.0%), 15 (8.5%), respectively. While in the age of 55 years and above, these clinical features were found as 5 (9.1%), 4 (7.3%), 4 (7.3%), 1 (1.8%), 5 (9.1%) respectively and were statistically non-significant (P=0.096). Positive Hess test was found 26 (12.3%) in the children (≤18 years),69 (22.6%) had in the young age group (19 – 36 yrs), was positive 57 (31.0%) in the middle age group(37 – 54yrs), while in the older age group (≥55 yrs) was noted 13 (23.6%) and was found non significant (P<.005). Gum bleeding, epistaxis, and bleeding from the GIT (melena and hemetemesis) were observed in all age groups with different proportions, 18 (8.5%), 14 (6.6%), and 1 (.5%) were found respectively in children, and the results were statistically non-significant (P=0.200). In young age groups (19 – 36 years), these features were noted as 40 (13.1%), 26 (8.5%), and 1 (0.3%), respectively. In the middle age (36 – 54yrs) were seen 22 (12.0%), 11 (6.0%), 0 (.0%) respectively, while in the older age group (≥55 yrs) were stated as 3 (5.5%), 1 (1.8%), 0 (0.0%) respectively and were statistically non significant (P=0.200). Retro orbital pain was found common in the young age group (19-37 yrs) and observed 93 (30.5%), 36 (17.0%) in children, 34 (18.5%) was in age group (37 – 54 yrs) and 11 (20.0%) in the elderly patients (≥55 yrs) and was found statistically

significant (P=0.001). Chills and rigors highly were observed in the children 78 (36.8%), in young age (19 – 36yrs) patients it was found 91 (29.8%), in the middle age patients (37 – 54 yrs) found 63 (34.2%), while in elderly patients it was found 16 (29.1%) and was noticed as non significant (P= 0.353). Loss of appetite was observed in children as 60 (28.3%), while in young age group(19 – 36yrs) were found 71(23.3%), 67 (36.4%) was observed in the middle age (37 – 54 yrs), while in the elderly (≥55yrs) patients loss of appetite was observed 23(41.8%) and was statistically significant (P=0.003).

Cough was present in children 62 (29.2%), in young (19 – 36yrs) was observed 60 (19.7%), in the patients of middle age (37 – 54 yrs) was noted 33 (17.9%), in the elderly noticed 11(20.0%) and was statistically significant (P=0.025). Nausea was observed in children as 39 (18.4%), in young age it was found 58 (19.0%), in middle age (36 – 54 years) it was 45 (24.5%), in elderly patients it was 17 (30.9%) and was found non-significant (P=0.104). Vomiting was found to have high in children and was present 121 (57.1%), in the young age group (19 - 36yrs) was mentioned 119 (39.0%), in the middle age(37 – 54yrs) 58 (31.5%), while in the elderly (≥55yrs) it was found as 20 (36.4%) and was statistically significant (P=<0.001). The details are demonstrated in Table 1.

The prevalence of the diseases DF, DHF and DSS was evaluated in different age groups. Dengue fever (DF) in this one year showed the highest proportion in ≥55 and less than 18 years of age, and DHF were more prevalent in the young age groups (19 – 36 yrs). The details are demonstrated in Table 2.

Complications were studied generally, as myocarditis was found (0.7%), encephalitis (0.9%), tachycardia (0.4%), bradicardia (0.4%), ascites (1.7%), and Jaundice (1.2%), Table 3.

Table 1: Clinical manifestations distribution of dengue fever in the age groups

***Fisher's exact test**

Clinical manifestations	Children ≤ 18 yrs n (%)	Young (19-36 yrs) n (%)	Middle age 37-54 yrs n (%)	Elderly ≥ 55 yrs n (%)	P-value

Fever	212 (100)	305 (100)	184 (100)	55 (100)	**---**
Arthralgia	43 (20.3)	160 (52.5)	104 (65.5)	24 (43.6)	**<.001**
Myalgia	53 (25.0)	195 (63.9)	110 (59.8)	26 (47.3)	**<.001**
Island of white in the Sea of red	4 (1.9)	8 (2.6)	11 (6.0)	5 (9.1)	**0.096**
Macular popular rashes	12 (5.7)	28 (9.2)	12 (6.5)	4 (7.3)	
Hess test	26 (12.3)	69 (22.6)	57 (31.0)	13 (23.6)	**<.001**
Gums bleeding	18 (8.5)	40 (13.1)	22 (12.0)	3 (5.5)	**0.200**
GIT(haematemesis and melena)	1 (.5)	1 (.3)	0 (.0)	0 (.0)	
Retro orbital pain	36 (17.0)	93 (30.5)	34 (18.5)	11 (20.0)	**0.001**
Epigastric pain	98 (46.2)	128 (42.0)	64 (34.8)	19 (34.5)	**0.094**
Chill/rigours	78 (36.8)	91 (29.8)	63 (34.2)	16 (29.1)	**0.353**
Loss of appetite	60 (28.3)	71 (23.3)	67 (36.4)	23 (41.8)	**0.003**
Cough	62 (29.2)	60 (19.7)	33 (17.9)	11 (20.0)	**0.025**
Nausea	39 (18.4)	58 (19.0)	45 (24.5)	17(30.9)	**0.104**
Vomiting	**121 (57.1)**	**119 (39.0)**	**58 (31.5)**	**20 (36.4)**	**<.001**

Table 2: Frequency of DF, DHF and DSS according to Age

Age	DF	DHF	DSS
≤18	145 (68.4%)	66 (31.1%)	**1 (.5%)**
19 – 36	197 (64.0%)	106 (34.8%)	**2 (.7%)**
37 – 54	112 (60.9%)	70 (38.0%)	**2 (1.1%)**
≥55	39 (70.9%)	15 (27.3%)	**1 (1.8%)**
Total	**493 (65.2%)**	**257 (34.0%)**	**6 (.8%**

Table 3: Complications of dengue fever found in hospitalised patients

Types of complications in patients	Percentage N (%)

	5 (0.7%)
Myocarditis	**7 (0.9%)**
Encephalitis	**3 (0.4%)**
Tachycardia	**3 (0.4%)**
Bradycardia	**13 (1.7%)**
Ascites	**9 (1.2%)**
Jaundice	**25 (3.3%)**
Pleural infusion	

DISCUSSION

Fever was present in all 756 admitted patients. Age was distributed as ≤ 18 age was defined as children, (19 -36 yrs) were called young, (37 – 54 yrs) middle age and (≥55 yrs) were considered as elderly. Arthralgia and myalgia were significantly present in all age groups in our study. However, arthralgia was observed significantly higher, 65.5%, in the middle age group, while myalgia was found significantly higher, 63.9%, in the young group (P <0.001). Agreeable results were found in another study in which adults had higher myalgia 83% and arthralgia 82% symptoms of disease (Harris *et al*., 2000).

In our results, symptoms like an island of white in the sea of red, macular popular rashes, were present, none significantly, in all age groups. These symptoms were predominant in the young age groups with percentages of 2.6%, 9.2%, respectively, except the condition of 'island of white in the sea of red', which was found higher in the elderly patients. In children, dengue-like symptoms may not be prominent in adults (Chadwick *et al*., 2006). In their study, has stated that the presence of myalgia, flushing, macular popular rashes or scattered petechiae was the most predictive feature of dengue fever as other non-dengue diseases. Similar symptoms were prevalent in the study evaluated in a hospitalised patient in children, were noted in 62%, and in adults, were 64 % (Lum *et al*., 2002). In a study conducted by Harris, slightly conflicting results were obtained (rash in children was observed in 62%, while in adults it was noted in 56 % (Harris *et al*., 2000).

The Hesse test is used as a screening test for dengue infection. In our study Hess test was seen in all age groups and was statistically significant (P <.001). However, Hess tests are significantly higher in the middle-aged patients aged 37 – 54 years. Our results do not

agree with the findings found in the study carried out by Harris *et al*. (2000. It was reported in a study that positive tourniquet test among children in 98.1% for DHF and 63.3% for DF and it was concluded that tourniquet test is helpful in differentiation from other illnesses disease such as chikungunya (Nimmannitya *et al*., 1987). According to Hammond and Whichmann, in their study, they found that the findings of positive tourniquet tests were in similar frequency between adult and child groups admitted to the hospital, which may not support the identification of positive tourniquet tests as the only sign of severe adult infection. Therefore, a tourniquet test might be used as an additional simple diagnostic tool for both children and adults with dengue virus infection (Hammond *et al*., 2005; Whichmann *et al*., 2004).

In our study, gum bleeding and epistaxis were more common than gastrointestinal bleeding, hematemesis 0.5% and melena 1.3%, but these are important signs which are needed to be examined carefully. Gastrointestinal bleeding may be initially dormant and usually manifests as abdominal pain or tenderness, a distended abdomen, pallor, tachycardia or a drop in haematocrit without clinical improvement found in young patients rather than children (Lum, 1997). Bleeding was studied from various sites and was found in 72%, gum bleeding and epistaxis were the common bleeding manifestations, 40% (Singh *et al*., 2005). Lum and his colleague reported in their study that bleeding in children was present in 62% and adults was 64%(Lum *et al*., 2008). Retro-orbital pain was a common symptom of dengue in the present study and was statistically significant (P <.001). Retro orbital pain in the present study was found highly significant in the young age 30.5% of patients. In a study conducted by Lum *et al*. (2008 similar results were reported in which the retro orbital pain was found in 40% of children, while in adults noted in 51%. It was reported from the Lum *et al*. (2008 study that 83% had headaches in children, and in adults, 96%. 96%. In our results, headache, melena, retro-orbital pain, and hematemesis were found more in adults than in children. Similar results were observed in a study by Kittigul *et al*. (2007).

In this study, based on age groups, chills and rigours were assessed and found in all age groups statistically non significance. In children, 36.8% was comparatively found to be higher than the other age groups. Loss of appetite was found as a sign of dengue in our study. In all age groups was seen statistically significance (P=0.003). However, in elderly

patients, 41.8% was significantly higher than in the other age groups. Matching results were reported in a study in which the sign of loss of appetite was present in 78% of DF and 93% in DHF (Kalayanrooj *et al,* 1997). Cough was present significantly in all age group levels, however found significantly higher, 29.2%, in children (P=0.025). In adults, signs and symptoms of dengue were evaluated in a study conducted in Puerto Rico, 35% cough (Cobra *et al*., 1995).

Halstead observed a cough in his study of children. 21 % suffered from dengue. Nausea and vomiting were assessed in our study and were found in all age groups with statistically significant differences (Halstead *et al.*, 1965). Nausea was noted non-significantly high in elderly patients, 30.9%, while vomiting was found significantly (P=0.007) high in children, 57.1%, as compared to other age groups. Based on the present study findings, the clinicians should carefully evaluate and observe vomiting, nausea, and diarrhoea in the febrile phase of the disease to assess whether the patient needs hydration or hospitalisation. Nausea and vomiting were analysed in a study conducted by Kittigul *et al*. (2007 and found in children 50.2% and in adults 76.4%.

COMPLICATIONS

In complications myocarditis was found (0.7%), encephalitis (0.9%), tachycardia (0.4%), bradicardia (0.4%), ascites (1.7%), Jaundice (1.2%), in these complications myocarditis was found in 5 (0.7%), which mostly lead to the hypotension and circulatory failure. All the patients recovered except one, was died. This may be due to excess fluid might have been given in DSS status and producing fatal acute heart failure. This was discussed in a study conducted by Kularatna *et al*. (2005. In other studies, similar results were reported in which circulatory complications occurred (Kamath and Suchitra, 2006). In our study, 7 (0.9%) patients the encephalitis. In these patients were observed a change in mental status was observed. This may be due to many factors, such as shock, electrolyte disturbance, and Acute Liver Failure (ALF) might contribute to encephalopathy (Malavige *et al*., 2007). In another study, the reason for neurological manifestations contributing to cerebral oedema was, direct neurotropic effect of dengue virus resulting in encephalitis or encephalopathy, or secondary to hepatic dysfunction and metabolic derangements such as hypoglycemia and hyponatremia (WHO,1999; Lum *et al*.,1996; Hendarto and Hadinegoro,1992). Tachycardia 3 (0.4%) and bradycardia 3 (0.4%) were observed in our

results. These cardiovascular complications were reported in the study conducted by Kamath and Suchitra (2006. Ascites, the fluid collection, was found in our results 13 (1.7%), pleural effusion 25 (3.3%), which is an abnormal fluid collection. Jaundice was observed in 9 (1.2%) patients, which is an unusual characteristic of dengue. Hepatic involvement has been accepted in dengue, and serum albumin level is considered a prognostic marker (Nimmannitya *et al*., 1987). In another study, hepatic dysfunction may be multifactorial; the most important causes are prolonged shock-associated metabolic acidosis and disseminated intravascular coagulation (DIC) with resultant ischemic hepatitis (Nimmannitya *et al*., 1987; George *et al*, 1988; Mohan *et al*.,2000).

The total number of patients with dengue fever (DF) was 493 (65.2%), dengue hemorrhagic fever (DHF), 257 (34.0%) and DSS patients were noted 6 (0.8%). This could be due to the rise in the population in Penang. Here, it shows that the highest proportion of dengue victims were children. Almost similar results were reported by the Social Statistical Bulletin Peninsular Malaysia in 1973 and 1974 (Department of Statistics 1973, 1974) that most of the children's age was below 14 years. In 1973, over 50% of cases occurred in children below 14 years (Fang *et al*., 1984). In Malaysia, the worst dengue and dengue hemorrhagic fever outbreak occurred in 1982, with most cases occurring in the Chinese population over the age of 15 years.

CONCLUSION: The differences in clinical features between children and adults require further evaluation to find out and recognise the substantial factors involved. Dengue hemorrhagic fevers, dengue shock syndrome, ascites, Jaundice, Pleural infusion are complications; all these markers could be helpful to make an early diagnosis of dengue infection and on severity of infections, complications can be fatal for patients, which is required early identification in association with thoroughly monitoring and basic supportive care to save the life of the patients.

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