

RETROSPECTIVE STUDY OF DENGUE FEVER (DF) AND DENGUE HEMORRHAGIC FEVER (DHF) PATIENTS AT UNIVERSITY MALAYA MEDICAL CENTER, KUALA LUMPUR, MALAYSIA IN THE YEAR 2005

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Abstract. The aim of this retrospective study was to determine the number of dengue fever (DF) and dengue hemorrhagic fever (DHF) cases admitted to University Malaya Medical Center (UMMC) in the year 2005 together with their clinical presentations and epidemiology. The data for 2005 was collected from the medical records department of UMMC. A total of 1,279 cases were admitted in 2005 with DF (81%, n=1,040) and DHF (19%, n=239). January had the greatest number of cases of DF and DHF (22%, n=281) and April had the least (4%, n=49). The greatest number of DF cases (38%, n=392) were seen in the 20-29 year age group, while the greatest number of DHF cases (32%, n=76) were in the 10-19 year age group. In regard to race, the greatest number of cases were seen in Malays (48%, DF; 49%, DHF). Males were more commonly infected than females. The majority of patients infected were students (30%, n=385). All patients with DF and DHF presented with fever. The symptoms reported included nausea and vomiting, joint pain, gum bleeding and dehydration. The mean value hemoglobin, white blood cell count and platelet count were 14.4 g/dl, 4×10^3 /dl, 75×10^6 /dl, respectively for DF and 15.1 g/dl, 4×10^3 /dl, 52×10^6 /dl respectively for DHF. The majority of patients were treated with hydration therapy. There were three deaths reported, caused by dengue shock syndrome (DSS).

INTRODUCTION

Dengue is the most common mosquito-borne viral disease of humans that in recent years has become a major international public health concern. The World Health Organization (WHO) estimates that more than 2.5 billion people are at risk for dengue infection, and 50 million cases occur annually with 22,000 deaths (WHO, 2002). The dengue virus is an enveloped single stranded RNA virus of the family Flaviridae. There are four serotypes which share genetic and antigenic features, but infection with one serotype does not provide long-term protection against other serotypes. The principal vector is the day biting *Aedes aegypti*, which typically breeds in clean stagnant water in a wide variety of sites, including man-made containers in domestic and peri-domestic urban areas (Kumarasamy, 2006).

DF was first reported in Malaysia in 1902 and DHF in 1962. Since then, epidemics of dengue cases have been reported regularly. The first major Malaysian epidemic of DHF with severe manifestations occurred in 1973, with 969 reported cases and 54 deaths (Wallace *et al*, 1980). DHF, though endemic in the sixties, emerged as a major public health problem in Malaysia from 1973 onwards (Shekhar and Huat, 1992, 1993). Until the end of September 2005, 29,196 cases of dengue had been reported with 76 deaths. The increasing trend in the incidence of dengue infection is a cause for concern (Kumarasamy, 2006).

DF is characterized by fever which lasts from 5 to 7 days with two or more of the following symptoms: headache, retro-orbital pain, myalgia, arthralgia, rash, hemorrhagic manifestations, or leukopenia.

DHF is defined as an acute febrile illness with hemorrhagic manifestations (shown by a positive tourniquet test, petechiae, ecchymoses or purpura, or bleeding from the mucosa, gastrointestinal tract, injection sites, or other locations), a platelet

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count $<100,000/\text{mm}^3$ and objective evidence of plasma leakage due to increased vascular permeability, shown by either a fluctuation in hematocrit $\geq 20\%$ during the course of illness and recovery or clinical signs of plasma leakage, such as pleural effusion, ascites, or hypoproteinemia (WHO, 1997).

The main objective of this retrospective study was to determine the number of DF and DHF cases admitted to the UMMC for the year 2005 and note their clinical presentations and epidemiology.

MATERIALS AND METHODS

The case records of all patients admitted with DF and DHF to the UMMC in the year 2005 were reviewed in detail. The data collected included date

of admission, age, sex, race, nationality, address, occupation, clinical presentations, laboratory investigation and treatment. Analysis was done using SPSS 11 and Microsoft Excel 2003.

RESULTS

A total of 1,279 cases were reported at UMMC for the year 2005. Eighty-one percent ($n=1,040$) of reported cases was DF and 19% ($n=239$) were DHF, giving a DF to DHF ratio of 4:1.

The greatest number of reported cases of DF were in the age group of 20-29 years (38%, 329 cases) and of DHF were in the age group of 10-19 (32%, 76 cases) (Fig 1).

Fig 2 shows the total number of DF and DHF cases by month. The greatest number of cases were reported in January (22%, $n=281$); 22%

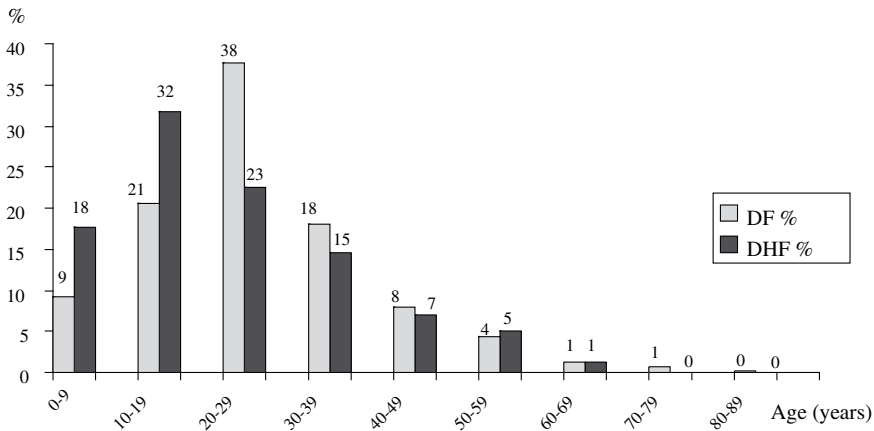


Fig 1- Age distribution of DF and DHF.

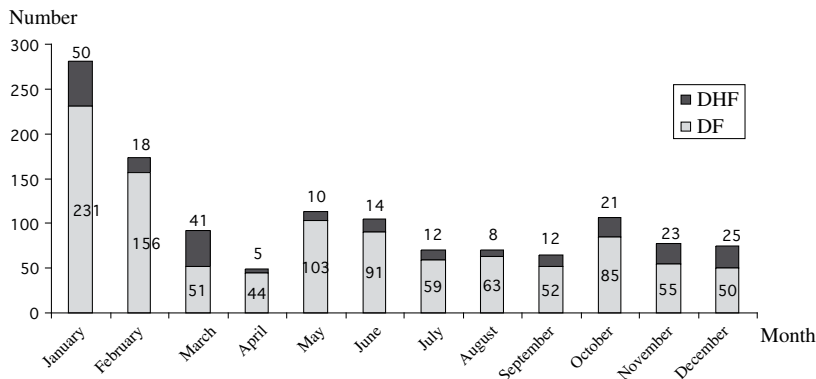


Fig 2- Number of DF and DHF cases by month.

Table 1
Socio-demographic characteristics cases with of DF and DHF.

Variables		DF		DHF		Total		p-value
		n	%	n	%	n	%	
Race	Malay	497	48	118	49	615	48	0.813
	Chinese	231	22	49	21	280	22	
	Indian	184	18	46	19	230	18	
	Others	128	12	26	11	154	12	
Sex	Male	614	59	148	62	762	60	0.412
	Female	426	41	91	38	517	40	
Nationality	Malaysian	919	88	213	89	1,132	89	0.741
	Non-Malaysian	121	12	26	11	147	11	
Dengue serology result	Positive	779	75	204	85	983	77	0.002 ^a
	Negative	121	12	13	6	134	10	
	Unknown	140	13	22	9	162	13	

^a Chi-square test is significant at $\alpha=0.05$ level

Table 2
Occupations among DF and DHF patients.

Occupation	No.	%
Student	385	30.1
Factory worker	54	4.2
Housewife	46	3.6
Teacher	22	1.7
Soldier	20	1.6
Restaurant worker	18	1.4
Businessman/woman	18	1.4
Maid	17	1.3
Contractor	17	1.3
Technician	14	1.1
Clerk	14	1.1
Pensioner	13	1.0
General worker	13	1.0
Salesman	12	0.9

(n=231) of the total were DF cases and 21% (n=50) were DHF cases. The fewest number of dengue cases was reported in April (4%, n=49) with 4% (n=44) of the total were DF cases and 2% (n=5) were DHF cases.

Table 1 shows the majority of DF and DHF cases were reported among ethnic Malays, males and Malaysian citizens. The dengue serology test

was positive in 77% (n=983). In 13%, the results of the dengue serology test were unavailable (unknown).

All patients with DF and DHF reported fever. Nausea and vomiting, joint pain, gum bleeding and dehydration were significantly associated with DF and DHF (p-value 0.004, 0.043, 0.003, and 0.001, respectively) (Table 3).

Hydration therapy was the commonest treatment. Paracetamol was prescribed to all patients. Platelet transfusions were given to DHF patients when needed. Three patients died due to complications of DHF.

Table 4 shows that the mean (standard deviation) hemoglobin, white blood cell count and platelet count were 14.4 ± 1.8 g/dl, $4.19 \pm 2.87 \times 10^3$ /dl, $75.53 \pm 50.83 \times 10^6$ /dl, respectively for DF and 15.1 ± 2.0 g/dl, $4.42 \pm 2.70 \times 10^3$ /dl, $51.86 \pm 41.01 \times 10^6$ /dl for DHF, respectively. However, data were missing for platelet count on 2 cases and for hemoglobin and white blood cell count on 3 cases.

DISCUSSION

The ratio of DF:DHF cases for the year 2005 at UMMC was 4:1. This is lower than that reported by the Ministry of Health (MOH), Malaysia. The ratio of DF:DHF for years 1996

Table 3
Symptoms of DF and DHF.

Symptoms		DHF		DF		Total		p-value
		n	% within case	n	% within case	n	% within case	
Fever	yes	239	100.0	1,040	100.0	1,279	100.0	.a
	no	0	0.0	0	0.0	0	0.0	
Myalgia	yes	117	49.0	442	42.5	559	43.7	0.710
	no	122	51.0	598	57.5	720	56.3	
Headache	yes	113	47.3	434	41.7	547	42.8	0.128
	no	126	52.7	606	58.3	732	57.2	
Nausea and vomiting	yes	183	76.6	696	66.9	879	68.7	0.004 ^b
	no	56	23.4	344	33.1	400	31.3	
Petechia	yes	62	25.9	200	19.2	262	20.5	0.260
	no	177	74.1	840	80.8	1,017	79.5	
Rash	yes	80	33.5	353	33.9	433	33.9	0.940
	no	159	66.5	687	66.4	846	66.1	
Cough	yes	48	20.1	199	19.1	247	19.3	0.717
	no	191	79.9	841	80.9	1,032	80.7	
Abdominal pain	yes	101	42.3	272	26.2	373	29.2	0.000 ^b
	no	138	57.7	768	73.8	906	70.8	
Joint pain	yes	62	25.9	207	19.9	269	21.0	0.043 ^b
	no	177	74.1	833	80.1	1,010	79.0	
Gum bleeding	yes	61	25.5	176	16.9	237	18.5	0.003 ^b
	no	178	74.5	864	83.1	1,042	81.5	
Dehydration	yes	94	39.3	297	28.6	391	30.6	0.001 ^b
	no	145	60.7	743	71.4	888	69.4	

^aNo statistics were computed because fever was a constant.

^bChi-square test is significant at $\alpha=0.05$ level

Table 4
Mean hemoglobin, white blood cell count and platelet count.

Cases		Hemoglobin (g/dl)	WBC (x10 ³ /dl)	Platelet count (x10 ⁶ /dl)
DF	Mean	14.4	4.19	75.53
	n	1,037	1,037	1,038
	Std deviation	1.8	2.87	50.83
DHF	Mean	15.1	4.42	51.86
	n	239	239	239
	Std deviation	2.0	2.70	41.01
Total	Mean	14.5	4.23	71.10
	n	1,276	1,276	1,277
	Std deviation	1.8	2.84	49.99

and 1997 were 26:1 and 23:1, respectively (MOH, 1996 and 1998). This may be because the area covered in this study was small, mostly Selangor and Kuala Lumpur, compared to MOH which covered all the states of Malaysia.

Our study showed the 20-29 years age group had the greatest number of cases of DF (38%, n=329) and the 10-19 years age group had the greatest number of cases of DHF (32%, n=76). The MOH for Malaysia also reported similar findings. They found the 15-29 year old age group had the highest incidence rate for DF (MOH, 2000). Fang *et al* (1984) reported that most cases were over age 15 years. These studies are different from the epidemics of the 1970s and 1980s, where the majority of cases were children below age 15 years old (Wallace *et al*, 1980; Hussin *et al*, 2005). DHF is primarily a disease of children under 15 years in hyperendemic areas (Halstead *et al*, 2001).

January had the greatest number of DF and DHF cases with 22% (n=281) while the least was in April at 4% (n=49) (Fig 2). Hussin *et al* (2005) also reported similar findings with the greatest incidence in January and the least in May. Shekhar and Huat (1992-1993) reported a peak incidence in August for DHF cases. Wallace *et al* (1980) reported cases occurred mainly from May to September. Fang *et al* (1984) reported the majority of cases occurred from July to October. The MOH reported the high incidence of dengue was probably the result of an increase in breeding places at construction sites (MOH, 2000).

The cases reported to UMMC showed Malays as the most commonly affected ethnic group, followed by Chinese, Indians and others. They were the most common ethnic group admitted. Hussin *et al* (2005) and Jamaiah *et al* (2005) also reported similar findings. This differs from the MOH report that showed Chinese as the majority of cases with dengue (43%), followed by Malays (39%), and Indians (6.3%) (MOH, 1996). Shekhar and Huat (1992-1993) reported male Chinese as the commonest group affected with both DF and DHF. Wallace *et al* (1980) and Fang *et al* (1984) also reported that most cases occurred among Chinese.

The majority of DF and DHF patients were students (30%, n= 385), followed by factory

workers (4%, n=54) and housewives (3.6%, n=46) (Table 2). This is to be expected as most cases occurred in teenagers.

All patients (DF and DHF) in this study had fever. Hussin *et al* (2005) and Jamaiah *et al* (2005) also reported fever as the commonest symptom. However, according to the WHO, the clinical features of DF vary according to the age of the patient. Infants and young children may have a non-specific febrile illness with rash. Older children and adults may have either a mild febrile syndrome or the classical incapacitating disease, abrupt onset high fever, severe headache, pain behind the eyes, muscle and joint pains, and rash. DHF is a potentially deadly disease that is characterized by high fever, hemorrhagic phenomena and circulatory failure. The illness commonly begins with a sudden rise in temperature accompanied by facial flush and other non-specific constitutional symptoms of dengue fever. The fever usually continues for two to seven days and can be as high as 40-41°C, possibly with febrile convulsions and hemorrhagic phenomena (WHO, 2002). Petechial skin rash, epistaxis and gum bleeding were seen most commonly in mild and moderately severe cases of DHF (George and Duraisamy, 1981). Wallace *et al* (1980) reported hemorrhagic manifestations were observed in 67% of cases of DHF in General Hospital Kuala Lumpur, Malaysia.

In this study, there were three deaths. They died due to dengue shock syndrome (DSS). Mortality can be as high as 10-20% (over 40% if shock occurs) without early appropriate treatment, but it is as low as 0.2% in hospitals with staff experienced with the disease. Warning signs that dengue shock syndrome is impending include sustained abdominal pain, persistent vomiting, change in the level of consciousness (irritability or somnolence), a sudden change from fever to hypothermia, and a sudden decrease in platelet count (Innis, 1995; Rigau-Perez, 1998).

The mean value for hemoglobin, white blood cell count and platelet count were 14.4 g/dl, 4×10^3 /dl, 75×10^6 /dl, respectively for DF and 15.1 g/dl, 4×10^3 /dl, 52×10^6 /dl for, respectively DHF (Table 4). The mean platelet count for both DF and DHF were low compared to the normal value. Thrombocytopenia (<100,000/ml) constitutes one

of the most common clinical findings in the course of dengue disease (Halstead, 1982; Ramirez-Ronda and Garcia, 1994). Platelet levels tended to decline from a higher value on admission to lower levels over subsequent days, with the lowest being on day 6 of the fever (Ibrahim and Cheong, 1995). The mechanisms involved in the thrombocytopenia associated with dengue disease are not well known, however, it may be due to alterations in megakaryocytopoiesis and platelet production. This possibility is based on analysis of bone marrow biopsies from dengue patients, which demonstrated a decrease in marrow cellularity, including megakaryocytes (Nelson and Bierman, 1964; Nakao *et al*, 1989). These alterations could be due to the ability of dengue virus to infect human hematopoietic cells and impair progenitor cell growth (Nakao, 1989; Murgue *et al*, 1997).

Primary prevention of dengue mainly resides in eliminating or reducing the mosquito vector. Public spraying for mosquitoes is the most important aspect of vector control. Application of larvicides, such as Abate[®], to standing water is more effective in long term control of mosquitoes. Initiatives to eradicate pools of standing water (such as in flowerpots) have proven useful in controlling mosquito borne diseases. Promising new techniques have been recently reported from Oxford University on rendering *Aedes* mosquito pest sterile (Wikipedia, 2006).

Personal prevention consists of the use of mosquito nets, repellents, cover exposed skin, use DEET-impregnated bednets, and avoiding endemic areas. This is also important for malaria prevention (Wikipedia, 2006). The control of dengue outbreaks requires a multi-pronged effort by various government agencies (Poovaneswari and Lam, 1992).

ACKNOWLEDGEMENTS

We would like to express our appreciation to YBhg Prof Dato' Dr Mohd Amin Jalaludin, former Director of UMMC. Special thanks to the staff of the Medical Ethics Committee, UMMC and Mr Teh Ah Huat, Senior Manager, Patient Information Department, UMMC for furnishing us with the latest data.

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