~ CHAPTER 4 ~

THE PROFILE AND MANAGEMENT OF DENGUE PATIENTS

4.1 Overview

This chapter begins with a study on the profile of dengue patients for the 2002 dengue outbreak at the University Malaya Medical Centre (UMMC). In the section following this, the dengue patients are examined according to their *sex*, *race* and *age*. With the information on *age*, these patients are further categorized into groups of children and adults (variable *child or adult*) for further analysis. Frequency of the different clinical diagnosis of dengue infection is reported in Section 4.3. The subsequent Section 4.4 discusses the patients' *length of stay* at the hospital. The admission of dengue patients is examined in Section 4.5 wherein the admission criteria at the UMMC (i.e. *thrombocytopenia_50* and *haemoconcentration_50*) are studied for this context. The frequency and results of the dengue serology test (*final serology result*) are reported in Section 4.6. Section 4.7 discusses the fulfillment of the dengue *notification* requirement at the UMMC. Section 4.8 deals with the clinical and laboratory features of dengue infection in children and adults prior to any classification. The last part of the chapter attempts to understand the symptomatic difference between DF and DHF independently for child and adult patients. Differences between the pediatric and adult dengue patients are also inspected here.

4.2 Demographics of Patients

During the period of dengue outbreak for about three and a half months from mid-July to October 2002, UMMC registered around 734 suspected cases of dengue infection. The demographic profile of these patients is described hereinafter.

Figure 4.1:
Percentage distribution of cases by gender

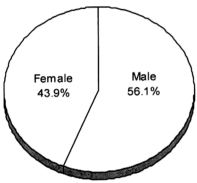
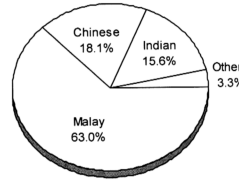


Figure 4.2:
Percentage distribution of cases by ethnicity



There were slightly more male than female in this outbreak with about 13 males to 10 females (Figure 4.1). Such has been the pattern observed in the period of 1992 to 1998 by Singh (2001).

Roughly three in every five patients were Malay (63%), while Chinese (18.1%) and Indian (15.6%) collectively made up about one third of the cases (33.7%) as illustrated in Figure 4.2.

Grouping the patients by their races (Table 4.1), it can be observed that there were more male than female in all the three main races, but not the other races. Indian

recorded the highest percentage of male patients at 71.1%, followed by Chinese at 59.1% and Malay 52.2%.

Table 4.1: Percentage distribution of cases by ethnicity and gender

		Ethnicity (%)				
		Malay	Chinese	Indian	Others	Total (%)
Gender	Male	52.2	59.1	71.1	43.5	56.1
	Female	47.8	40.9	28.9	56.5	43.9
Total		*100.0*	*100.0*	*100.0*	*100.0*	*100.0*
No. of Cases		462	132	114	23	731

The mean age for all suspected dengue cases in this study is about 21.64 years; fairly close to the median of 22 years. The age of patients ranges from a minimum of 1 to 83 years old. As seen in Figure 4.3, more than a third of the dengue patients (35.6%) are in their twenties (20 – 29 years old). Patients below 10 years old make up the second largest group at 21.4%, followed by teenagers (10 – 19 years old) at 20.9%. About 13.1% of the patients are in their thirties while 9% aged 40 and above. Some 89% of the cases are between the age of 5 to 55 who come mostly from the working and school-going groups. Since *Aedes* mosquitoes are known to be day-biters (Singh, 2001), this may correspond to the high outdoor[2] *Aedes* Index (Tham, 2001). Nevertheless, it is also noted that children age 1 to 4 make up about 9% of the total cases. The distribution of age is skewed to the right due partly to two subjects who were in their eighties. Shown in Table 4.2, the skewness and kurtosis values for the distribution of age do not suggest severe deviation from the normal distribution. The interquartile range for all cases runs from 12 to 29 years of age.

[2] By outdoor, it means premises other than homes. For example, schools, factories, construction sites and so on.

Figure 4.3: Frequency histogram of age group

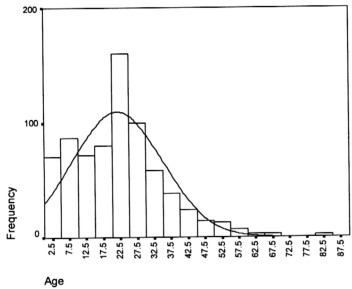
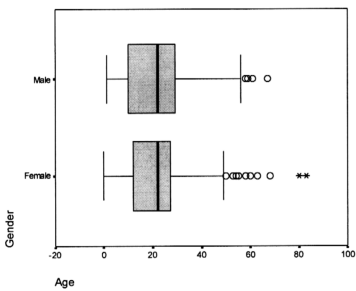


Table 4.2: Descriptive statistics of age for all cases (Valid N = 730)

		Statistics
Mean		21.64
Median		22.00
Standard Deviation		13.31
Minimum Value		1.00
Maximum Value		83.00
Skewness		0.79
Kurtosis		1.22
Percentile	25	12.00
	50	22.00
	75	29.00

Zooming into the age of patients by their gender, it was noted that the median age was the same for both gender (22 years) as depicted by the boxplot in Figure 4.4. The age of female patients was however more skewed to the right than that of the male due partly to the many outliers in the former gender. These outliers were retained in the analysis for they were non-problematic and were representative of the population. Interquartile range was wider for male (19 years) than it was for female patients (15 years).

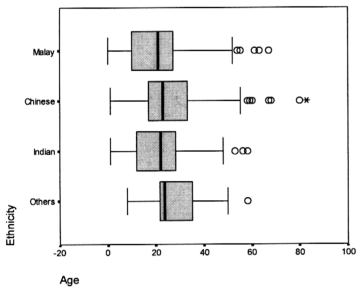
Figure 4.4: Boxplot of age by gender of patients



° Cases with values between 1.5 and 3 interquartile range from the upper and lower edge of the box
* Cases with values more than 3 interquartile range from the upper and lower edge of the box

At 23 years, the median age for Chinese was the highest compared to Malays at 21 years and Indians at 22 years as shown in Figure 4.5. The age groups for all races (including the other races) were skewed to the right due partly to the aforementioned outliers ranging from 50 to 80 over years old. The interquartile range for the three main races was fairly close to one another – about 16.5 to 17.5 years apart.

Figure 4.5: Boxplot of age by ethnicity of patients



Median:	Malay	= 21
	Chinese	= 23
	Indian	= 22
	Others	= 23.5
Range:	Malay	= 1 to 67
	Chinese	= 1 to 83
	Indian	= 1 to 58
	Others	= 8 to 58
Skewness:	Malay	= 0.577
	Chinese	= 1.023
	Indian	= 0.566
	Others	= 0.977

° Cases with values between 1.5 and 3 interquartile range from the upper and lower edge of the box
* Cases with values more than 3 interquartile range from the upper and lower edge of the box

Recognizing that certain dengue features may differ between the adults and children as advocated by the literature, it is necessary to segregate all cases into groups of children with age up to 12 years and adults beyond 12 years old. The suggested grouping is in accordance with the onset of puberty which normally begins from the average age of 12 years (Wikipedia, 2005).

In this study, the ratio of child to adult is about 7: 18 as observed in Figure 4.6. Further subdividing the pediatric and adult patients by their gender revealed more male in both groups (Table 4.3). Higher percentage of male was observed in children at 60.1%, while adult male made up about 54.6%.

Figure 4.6: Percentage distribution of cases by child and adult patients

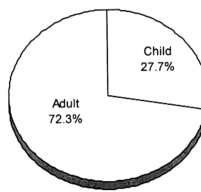


Table 4.3: Percentage distribution of child and adult cases by gender

		Child (%)	Adult (%)	Total (%)
Gender	Male	60.1	54.6	56.1
	Female	39.9	45.4	43.9
Total		*100.0*	*100.0*	*100.0*
No. of Cases		203	529	732

Malay made up the most in the child and adult category at 72.4% and 59.4% respectively (Table 4.4). There was almost an equal percentage of Chinese and Indian in the pediatric category at 12.3% and 14.8% respectively. In the adult cases, slightly more Chinese (20.4%) was observed than Indian (15.8%).

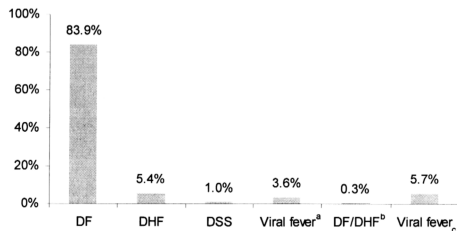
Table 4.4: Percentage distribution of child and adult cases by ethnicity

		Child (%)	Adult (%)	Total (%)
Race	Malay	72.4	59.4	63.0
	Chinese	12.3	20.4	18.1
	Indian	14.8	15.8	15.6
	Others	0.5	4.3	3.3
Total		*100.0*	*100.0*	*100.0*
No. of Cases		203	529	732

4.3 Clinical Diagnosis of Dengue

Depending on the clinical and laboratory presentations, patients suspected of dengue infection are basically diagnosed as having dengue fever (DF), dengue haemorrhagic fever (DHF), dengue shock syndrome (DSS) or the undifferentiated viral fever which might be due to viral infection other than dengue. For the UMMC experience of the 2002 outbreak, majority of the cases were classified as DF at 83.9% as shown in Figure 4.7. Those clinically diagnosed as DHF made up only about 5.4% of the total cases while DSS constituted a mere 1%. About 3.6% of the patients were diagnosed as having the undifferentiated viral fever while 0.3% had the indefinite DF or DHF symptoms. Those with non-dengue viral fever (shown as viral fever TRO DF in the bar chart) constituted about 5.7% of the total cases in this study.

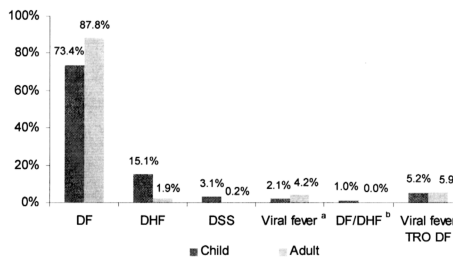
Figure 4.7: Percentage distribution of dengue patients by clinical diagnosis



[a] viral fever showing no differential symptoms as dengue fever
[b] indecisive between DF and DHF
[c] viral fever to rule out (TRO) dengue fever

Segregating the cases into groups of children and adults, it was noted (in Figure 4.8) that a greater percentage of children had the more severe DHF and DSS at 15.1% and 3.1% respectively vis-à-vis the adults at 1.9% and 0.2% for the respective categories. A relatively higher percentage of adults were diagnosed as DF (87.8%) as opposed to the children (73.4%). The percentages of children and adults diagnosed as having viral fever were 2.1% and 4.2% correspondingly. About 5.2 % of the children and 5.9% of the adults were ruled out of dengue infection. One percent of the children were unspecified between DF and DHF, while adults none.

Figure 4.8: Percentage distribution of child and adult dengue patients by clinical diagnosis



[a] viral fever showing no differential symptoms as dengue fever
[b] indecisive between DF and DHF
[c] viral fever to rule out (TRO) dengue fever

Tabulating the clinical diagnosis based on the gender of the patients (Table 4.5), it can be seen that for the DF cases, there were slightly more male (54.4%) than female (45.6%). Similarly, for the diagnosis of DHF and viral fever, male substantially outnumbered female at 69.2% and 61.5% versus 30.8% and 38.5% respectively. For those having viral fever with dengue ruled out, slightly more male was observed. Percentage was not computed for DSS and the indefinite cases of DF/DHF due to the small sample sizes which can produce biased estimates.

Across the different races, preponderance among Malays was evident in all categories of clinical diagnosis. For the same reason due to small sample size, percentages were not computed for DSS and the indefinite DF/DHF cases.

Table 4.5: Percentage distribution of clinical diagnosis by gender (N = 714)

Clinical Diagnosis	No. of Cases	Gender (%)		Total
		Male	Female	
DF	599	54.4	45.6	*100.0*
DHF	39	69.2	30.8	*100.0*
DSS *	7	-	-	*100.0*
Viral fever	26	61.5	38.5	*100.0*
DF/DHF *	2	-	-	*100.0*
Viral fever TRO DF	41	51.2	48.8	*100.0*

* The percentage is not represented due to small sample size.

Table 4.6: Percentage distribution of clinical diagnosis by ethnicity (N = 715)

Clinical Diagnosis	No. of Cases	Ethnicity (%)				Total
		Malay	Chinese	Indian	Others	
DF	600	63.3	17.8	15.5	3.3	*100.0*
DHF	39	66.7	20.5	12.8	0.0	*100.0*
DSS *	7	-	-	-	-	*100.0*
Viral fever	26	46.2	23.1	26.9	3.8	*100.0*
DF/DHF *	2	-	-	-	-	*100.0*
Viral fever TRO DF	41	68.3	14.6	14.6	2.4	*100.0*

* The percentage is not represented due to small sample size.

4.4 Length of Stay

The average length of stay for those admitted to the hospital was about three and a half days. Looking at the mean length of stay, although children appeared to stay slightly longer than adults, the Mann-Whitney *U* test for large samples did not provide sufficient evidence (p-value is 0.139) to substantiate a difference in the population distributions of the length of stay between children and adults. Note that the non-parametric test was chosen here due to the non-normality of the length of stay as noted in Table 4.7 which also provides other descriptive statistics. Nevertheless, the variability of the children's length of stay was greater as indicated by its larger standard deviation at 2.83 versus the adult's at 1.79. Similarly, while both groups have the same median of 3 days, children documented a larger interquartile range of 2.75 days (from the 1st to 3rd quartile) as opposed to the adult's of 2 days. At 27 days, the children's range of stay is more than double the adults' of 11 days.

Table 4.7: Length of stay for all admitted patients (N = 406), adult and child cases

	Mean	Std. Deviation	Median	Interquartile Range	Min	Max
Overall (N = 406)	3.45	2.22	3.00	2.00	1	28
Child [a] (N = 144)	3.70	2.83	3.00	2.75	1	28
Adult [a] (N = 262)	3.31	1.79	3.00	2.00	1	12

Kolmogorov-Smirnov test of normality on the length of stay for child/adult rejected at 5% with $p<0.01$.
[a] Mann-Whitney *U* test statistic, Z is -1.479 with p-value of 0.139.

Table 4.8 shows that the mean period of stay lengthens from 3.30 days for DF cases to 3.47 days for the more serious DHF cases. However, the Mann-Whitney *U* test did not provide sufficient evidence to suggest a significant difference in the length of stay between the DF and DHF patients. Those diagnosed as having viral fever with dengue ruled-out stayed around 3.3 days on average. Statistics for patients diagnosed with DSS, viral fever and DF/DHF were not computed due to the small sample size which might produce biased and misleading results.

Table 4.8: Length of stay by clinical diagnosis (N = 399)

	N	Mean	Std. Deviation	Median	Interquartile Range	Min	Max
DF [d]	331	3.30	1.82	3.00	2.00	1	16
DHF [d]	36	3.47	1.58	3.00	1.00	1	7
DSS *	7	-	-	-	-	-	-
Viral Fever [a] *	6	-	-	-	-	-	-
DF/DHF [b] *	2	-	-	-	-	-	-
Viral Fever TRO DF [c]	17	3.29	1.61	3.00	2.00	1	7

[a] viral fever showing no differential symptoms as dengue fever
[b] indecisive between DF and DHF
[c] viral fever to rule out (TRO) dengue fever

Kolmogorov-Smirnov test of normality on the length of stay for DF and DHF rejected at 5% with $p<0.01$.
[d] Mann-Whitney *U* test statistic, Z is -1.123 with p-value of 0.262.
* The statistics are not represented due to small sample size.

4.5 Admission of Dengue Patients

The overall admission rate at the UMMC for the period under study was 56.1%. More children were admitted than adults as seen in Table 4.9. In every 10 children clinically diagnosed as having dengue infection, about 7 were admitted in contrast to only 1 in 2 adults being admitted.

Table 4.9: Percentage distribution of child and adult by admission

		Child (%)	Adult (%)	Total (%)
Admitted	Yes	72.9	49.6	56.1
	No	27.1	50.4	43.9
Total		*100.0*	*100.0*	*100.0*
No. of Cases		203	528	731

Not all patients clinically diagnosed as DF were admitted. Findings in Table 4.10 show only about half (56%) of the clinical DF cases were admitted to the hospital. Almost all patients (92.3%) under the condition of DHF were admitted with a small portion of them not (7.7%). Despite the fact that all DSS patients were admitted, the percentage was not computed here as sample size was small. The same goes for DF/DHF. Only 16.7% of those with the less severe viral fever were admitted. Perhaps due to the complicated diagnosis, many patients with non-dengue disease (41.5%) were admitted for further surveillance and tests before ruling out the possibility of dengue.

Table 4.10: Percentage distribution of clinical diagnosis by admission

	Admitted (%)		Total (%)	No. of Cases
Clinical Diagnosis	Yes	No		
DF	56.0	44.0	*100.0*	600
DHF	92.3	7.7	*100.0*	39
DSS	-	-	-	7
Viral fever	16.7	83.3	*100.0*	24
DF/DHF	-	-	-	2
Viral fever TRO DF	41.5	58.5	*100.0*	41
Total	56.4	43.6	*100.0*	713

According to Chin (1993), two of the four admission criteria for patients diagnosed with dengue at the UMMC are those with platelet count of less than 50,000/mm^3 (thrombocytopenia) and hematocrit changes of greater than 50%.

Findings in this study suggest non-compliance of the admission protocol. Referring to Table 4.11, it is noted that 97.1% of the patients suffering platelet count of less than the suggested threshold were admitted, while the remaining 2.9% were missed out. Further investigation is required to understand the nature of such non-admission.

Table 4.11: Percentage distribution of admission and thrombocytopenia of 50,000 per mm^3 or less (column percentage)

	Thrombocytopenia_50 (%)	
Admission	Yes	No
Admitted	97.1	47.0
Not Admitted	2.9	53.0
Total	*100.0*	*100.0*
No. of Cases	136	574

Admission due to thrombocytopenia (<50,000/mm^3) constituted about 32.8% of total admission (Table 4.12), lower than the 58.6% as observed in the similar hospital study by Chin (1993). Hypothetically, if the admission criterion is amended to allow all patients with thrombocytopenia of less than 100,000/mm^3 be admitted, admission rate based solely on this criterion would be 51.4% (from the current 32.8%).

Table 4.12: Percentage distribution of admission and thrombocytopenia of 50,000 per mm^3 or less (row percentage)

	Thrombocytopenia_50 (%)		Total	No. of Cases
Admission	Yes	No		
Admitted	32.8	67.2	*100.0*	402
Not Admitted	1.3	98.7	*100.0*	308

All patients with raised hematocrit greater than 50% were admitted (Table 4.13) and admission of such cause made up about 4.1% of total admission (Table 4.14), in comparison to 19.2% as documented by Chin (1993). If the admission ceiling for hematocrit were to be reduced to 20%, the admission rate based solely on this reason would be 15.2%.

Table 4.13: Percentage cross-tabulation of admission and hematocrit change of 50% or more (column percentage)

	Haemoconcentration_50 (%)	
Admission	Yes	No
Admitted	100.0	55.0
Not Admitted	0.0	45.0
Total	*100.0*	*100.0*
No. of Cases	17	714

Table 4.14: Percentage cross-tabulation of admission and hematocrit change of 50% or more (row percentage)

	Haemoconcentration_50 (%)			
Admission	Yes	No	Total	No. of Cases
Admitted	4.1	95.5	*100.0*	410
Not Admitted	0.0	100.0	*100.0*	321

With the currently admission rate of 56.1%, there were clearly admissions of other reasons which required further investigation in order to assess the adequacy of such admission rate seeing that over-admission might take a toll on the efficiency of the hospital while under-admission translates to ineffectiveness of patient management.

4.6 Dengue Serology Test

Not all clinically diagnosed patients were serologically tested for the dengue virus. In this study, roughly three out of five suspected cases (62.3%) were tested via the laboratory serology method, while the rest was not as shown in Figure 4.9. Of this percentage, 65% of them turned out positive. This percentage is on the high side if compared to the proportion of laboratory confirmed dengue cases over all clinically diagnosed cases that ranges from 40.9% to 50.2% for the period of 1995 to 1999 at the national level (Singh, 2001).

Figure 4.9: The percentage of clinical cases tested serologically and the result breakdown

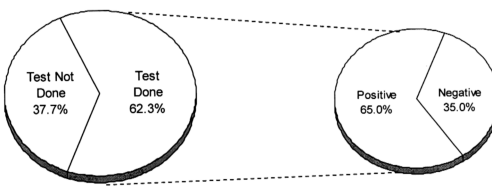
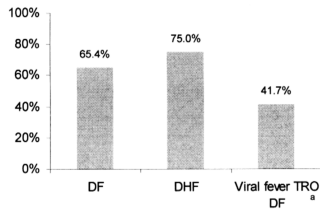


Figure 4.10 shows that slightly more DHF cases (75.0%) were tested positive serologically as compared to the DF cases at 65.4%. Ironically, albeit the ruling-out of dengue fever by the initial clinical diagnosis, some 41.7% of the patients from this category was diagnosed positive. Percentages for the DSS, viral fever and indefinite DF/DHF were not computed as sample size is too small as explained earlier.

Figure 4.10: Percentage of positive dengue serology result by clinical diagnosis*



[a] viral fever to rule out (TRO) dengue fever
* Percentage is not shown for DSS, Viral Fever and DF/DHF due to small sample size.

4.7 Notification of Clinical Dengue Cases

Under the Prevention and Control of Infectious Diseases Act, 1988, dengue is made a notifiable disease. All clinically diagnosed cases are to be notified to the nearest District Health Office within 24 hours, with or without laboratory confirmation. The data from this study reveal some 45.5% of the clinical dengue cases were not notified (Table 4.15). The rest was mostly notified as DF at 48.0% while DHF only made up about 6.4%.

Table 4.15: Frequency and percentage distribution for the notification of DF/DHF to the District Health Office

Notification	Frequency	Percent
Notified as DF	343	48.0
Notified as DHF	46	6.4
Not Notified	325	45.5
Total	714	100.0

Table 4.16 shows that more than half (61.6%) of the total cases not notified were positive of dengue infection. For cases notified as either DF or DHF, about 65% to 66% turned out positive.

Table 4.16: Percentage distribution of DF/DHF notification and final dengue serology test results (row percentage)

	Serology Result (%)			
	Positive	Negative	Total (%)	No. of Cases
Not notified	61.6	38.4	100.0	343
Notified as DF	65.3	34.7	100.0	46
Notified as DHF	65.9	34.1	100.0	325

The findings above highlight severe slack in the compliance of the disease notification which should be looked into and possibly rectified at once to ensure a responsive dengue surveillance and control system.

4.8 Clinical and Laboratory Observation of Child and Adult Dengue Patients

The objective of this section is to look at the frequencies of the various symptoms related to dengue infection prior to any diagnosis or classification attempt. The tabulation was divided into groups of children and adults in recognition of the symptomatic differences between the two groups. Pearson Chi-Squares were computed to assess the independence between child/adult and the various symptoms. The odds ratios together with the confidence bands were calculated to study the relative risk of adult and child (child coded as 1; adult as 0) in relation to the dengue symptoms (coded 1 as positive, 0 otherwise).

Table 4.17 shows the percentages of the observed symptoms in adults and children suspected of dengue infection. Almost all patients cited fever (over 90% of child and adult patients), which is typical of such viral infection. Some commonly observed clinical manifestations include skin rashes / petechiae (in almost 70% of children and 49% of adults), vomiting (about 50% for both), muscle and joint pain (41% of children and 68% of adults), dehydration (41% of children and 31% of adults) and headache (35% of children and 47% of adults).

Thrombocytopenia_100 (dichotomized at 100,000 platelet count per mm^3) was fairly common especially in adults at 56% versus the children of 38%. Children had about half the odds (0.477) over adults in observing platelet count of 100,000 per mm^3 or less. More adults (68%) than children (41%) complained about the pain of muscle and joint. Again, the odds of children recording such symptoms were about one third of the adults (0.322).

On the other hand, a greater proportion of children (44%) experienced shock in this outbreak. The calculated odds of observing shock in children were about 65 times of that in adults! Partly by reason of that, they also registered relatively higher percentage of giddiness, shock, hepatomegaly, abdominal pain, dehydration, *haemoconcentration_20* and *haemoconcentration_50*. It should be noted that haemoconcentration is an indication of plasma leakage that if untreated, might lead to shock syndrome.

Table 4.17: Percentage of clinical and laboratory findings of child and adult clinically diagnosed as having dengue infection

Symptom	No. of Cases		% Positive		Pearson Chi-Square [a]	Odds Ratio	95% Confidence Interval
	Child	Adult	Child	Adult	P-value [b]		
Fever	203	531	91	93	0.473	0.770	(0.428, 1.386)
Vomit	193	530	53	50	0.614	1.104	(0.794, 1.536)
Giddiness	193	528	26	19	0.050*	1.500	(1.020, 2.207)
Headache	20	166	35	47	0.436	0.607	(0.231, 1.599)
Skin Rash	23	169	70	49	0.105	2.368	(0.927, 6.051)
Eye Pain	22	169	9	17	0.552	0.504	(0.111, 2.277)
Muscle & Joint Pain	22	170	41	68	0.022*	0.322	(0.130, 0.800)
Bleeding	192	522	19	18	0.827	1.073	(0.704, 1.636)
Shock Evidence	23	170	44	1	0.000**	64.615	(12.79, 326.39)
Hepatomegaly	193	525	15	3	0.000**	4.780	(2.577, 8.864)
Rash / Petechiae	22	164	64	49	0.279	1.838	(0.732, 4.616)
Abdominal Pain	193	527	28	20	0.027*	1.561	(1.068, 2.283)
Dehydration	192	527	41	31	0.013*	1.561	(1.109, 2.197)
Thrombocytopenia_50[c]	192	521	15	21	0.113	0.680	(0.435, 1.065)
Thrombocytopenia_100[c]	192	521	38	56	0.000**	0.477	(0.340, 0.670)
Haemoconcentration_20[d]	200	528	28	10	0.000**	3.414	(2.248, 5.148)
Haemoconcentration_50[d]	203	531	5	1	0.008**	3.879	(1.456, 10.333)

[a] With continuity correction.
[b] Two-sided asymptotic significance. * significant at 5%; ** significant at 1%.
[c] Created by dichotomizing variable platelet count at admission at 100,000 and 50,000 per mm^3
[d] Created by dichotomizing variable hematocrit change at 20% and 50% respectively

For symptoms measured on a numerical scale, Table 4.18 provides the results of the Mann-Whitney *U* test for assessing the equality of population distributions between the child and adult patients for a specific dengue symptom. Except for fever duration, the results suggest that heart rate, platelet count at admission and hematocrit change are different between child and adult patients in this dengue outbreak at UMMC.

Table 4.18: Mann-Whitney *U* test for symptoms grouped by child or adult

Symptoms	Mann-Whitney *U* test P-value [a]
Fever Duration	0.409
Heart rate per minute	0.000
Platelet count at admission	0.000
Hematocrit change (%)	0.000

[a] P-value for 2-tailed test.
Kolmogorov-Smirnov test of normality for all symptoms grouped by child or adult rejected at 5% with $p<0.01$.

4.9 Clinical Diagnosis of DF/DHF and the WHO Guidelines

To study if the clinical diagnosis by the medical officers conforms to the prescribed WHO guidelines, a new set of "imaginary" diagnosis (variable *WHO Diagnosis*) was created by the owner of the dataset. This was done based strictly on the patient's information on *thrombocytopenia_100* and *haemoconcentration_20*. A patient is diagnosed as having DHF if and only if both of the said laboratory findings are present.

With this "re-diagnosis", the cross-tabulation of the clinical diagnosis (by the medical officers) versus the newly created *WHO Diagnosis* in Table 4.19 offers some insights in relation to the conformity of the WHO guideline when diagnosing patients suspected of dengue. In this study, there were 54 cases potentially under-diagnosed as

DF when they should be DHF. On the other hand, about 24 cases were probably over-diagnosed as DHF when they ought to be DF. There was one DSS case which should be diagnosed as DF instead. Two cases of viral fever TRO DF exhibit symptoms of DHF as per the WHO guidelines and as such, should be treated as DHF instead. These numbers suggest that about 11.4% [(54+24+1+2) / 712] of the clinical cases were somehow "mis-diagnosed". Although there were 26 cases of viral fever and 39 cases of viral fever to-rule-out (TRO) DF that should be DF instead, the intertwining complexity of dengue and other viral fevers necessitates a detail review of these cases on an individual basis to ascertain the appropriateness and adequacy of the original diagnosis. The nonconformity illustrated here requires further study to understand the nature of such non-compliance.

Table 4.19: Cross-tabulation of clinical diagnosis and diagnosis as per the WHO guideline

	WHO Diagnosis		
Clinical Diagnosis	DF	DHF	Total
DF	543	54	597
DHF	24	15	39
DSS	1	6	7
Viral fever [a]	26	0	26
DF/DHF [b]	1	1	2
Viral fever TRO DF [c]	39	2	41
Total [d]	634	78	712

[a] viral fever showing no differential symptoms as dengue fever
[b] indecisive between DF and DHF
[c] viral fever to rule out (TRO) dengue fever
[d] exclude 22 missing cases

The reclassification of DF and DHF via the variable *WHO Diagnosis* as explained earlier makes it possible to examine the symptomatic differences of DF and DHF as per the WHO guideline, instead of using the original clinical diagnosis which might have some inconsistencies with the guidelines as demonstrated. The comparisons between the symptoms of DF and DHF (independently for child and adult patients) are presented in Table 4.20. It is warned that due to the small sample size of certain categories, interpretation of the percentages provided in the table must be made with great caution.

For children, those classified as DHF (as per the WHO guide) exhibited higher percentage of vomiting, hepatomegaly, abdominal pain, dehydration, (and of course) thrombocytopenia and haemoconcentration (both of which are the WHO criteria for DHF). Likewise, adult DHF cases also reported higher incidence of the same symptoms, except for hepatomegaly and dehydration. In addition, bleeding was more commonly observed in adult DHF patients.

Comparing the dengue manifestations in the DHF children of this study to the 34 DHF pediatric cases during the 1982 outbreak (Table 2.3) at the similar hospital (Taib et al., 1983), it is noted that the occurrence of fever and thrombocytopenia (100,000 per mm^3 or lower) is fairly comparable between the two episodes. However, the percentage of hepatomegaly is lower in this study at 27% versus the 95% in the 1982 outbreak. On the other hand, all children in this study had petechiae and haemoconcentration (at 100% each) vis-à-vis the 53% and 32% respectively for the 1982 outbreak.

For adults diagnosed as having DHF (cross reference with Table 2.2), fever was as common in the 1982 outbreak (87%) as it was in this study (90.7%). All adult DHF patients suffered thrombocytopenia (100,000 per mm^3 or lower) in both outbreaks. Lower percentage of DHF adults documented petechiae (44.8%) and hepatomegaly (4.8%) in this study in contrast to the 60% and 67% respectively in the 1982 outbreak. Haemoconcentration (hematocrit changes of 20% or more) was more prevalent among the DHF adults in this study (100%) versus the 1982 outbreak (40%).

Table 4.20: Percentage of clinical and laboratory findings for the DF and DHF cases diagnosed as per the WHO guideline[b] grouped by child and adult

	No. of Child		No. of Adult		Child (%)			Adult (%)		
Symptom	DF	DHF	DF	DHF	DF	DHF	Sig.[a]	DF	DHF	Sig.[a]
Fever	160	40	485	43	92.5	92.5		93.6	90.7	
Vomit	155	37	484	43	47.1	78.4	**	49.0	69.8	*
Giddiness	155	37	483	42	24.5	35.1		19.9	14.3	
Headache	17	3	137	29	35.3	33.3		46.7	48.3	
Skin Rash	20	3	139	30	70.0	66.7		51.1	40.0	
Eye Pain	19	3	140	29	10.5	0.0		17.1	13.8	
Muscle & Joint Pain	19	3	141	29	42.1	33.3		68.1	69.0	
Bleeding	154	37	479	40	17.5	27.0		16.5	40.0	**
Shock Evidence	20	3	141	29	35.0	100.0		0.7	3.4	
Hepatomegaly	155	37	480	42	11.6	27.0	*	3.3	4.8	
Rash / Petechiae	19	3	135	29	57.9	100		49.6	44.8	
Abdominal Pain	155	37	482	42	24.5	43.2	*	18.5	38.1	**
Dehydration	154	37	481	43	35.1	67.6	**	30.6	37.2	
Thrombocytopenia_50	154	37	479	42	3.2	62.2	**	16.9	64.3	**
Thrombocytopenia_100	154	37	479	42	22.7	100.0	**	52.4	100.0	**
Haemoconcentration_20	160	40	485	43	10.0	100.0	**	2.3	100.0	**
Haemoconcentration_50	160	40	485	43	1.9	17.5	**	0.2	14.0	**

[a] Pearson χ^2 test of independence for *WHO diagnosis* and symptom significant at * 5% or ** 1% with continuity correction.

[b] Diagnosis of DHF is supported by laboratory findings of thrombocytopenia (platelet count <100,000/mm^3) and haemoconcentration (hematocrit changes > 20%).

Re-tabulating the dengue symptoms (Table 4.21), this time not according to the WHO guidelines but the clinical diagnosis by the medical doctors, shows that majority of the children suffering thrombocytopenia and haemoconcentration were clinically diagnosed as DHF. Those with the said symptoms but clinically diagnosed as DF might not have them concurrently – a pre-requisite for diagnosis of DHF. Symptoms such as vomit, hepatomegaly, abdominal pain and dehydration were significantly different between the DF and DHF pediatric patients, likewise observed in the diagnosis as per the WHO guideline in Table 4.20. Bleeding was more common in the clinical DHF than DF children. Shock evidence was not shown to be different between the clinical pediatric DF and DHF possibly due to the small sample size.

For the adult patients, there wasn't much symptomatic distinction between the clinical DF and DHF. Incidence of bleeding and evidence of shock appear to differ significantly between the clinical adult DF and DHF. Still, the small sample size necessitates a careful interpretation of such findings. The fact that thrombocytopenia and haemoconcentration were not significantly different between the two clinical diagnoses (as they should have been as shown previously in Table 4.20) suggests that the WHO guidelines were not consistently applied during the clinical diagnosis of the adult dengue patients (which possibly resulted in a smaller number of DHF cases).

Table 4.21: Percentage of clinical and laboratory findings for the DF and DHF cases clinically diagnosed by the medical doctors grouped by child and adult

	No. of Child		No. of Adult		Child (%)			Adult (%)		
Symptom	DF	DHF	DF	DHF	DF	DHF	Sig.[a]	DF	DHF	Sig.[a]
Fever	141	35	460	11	94.3	100.0		92.6	100.0	
Vomit	141	35	459	11	46.8	77.1	**	50.8	72.7	
Giddiness	141	35	458	11	23.4	40.0		19.9	36.4	
Headache	13	7	147	2	30.8	42.9		44.9	50.0	
Skin Rash	14	8	149	3	78.6	62.5		51.7	33.3	
Eye Pain	14	8	150	2	7.1	12.5		17.3	0.0	
Muscle & Joint Pain	14	8	151	2	42.9	37.5		68.9	100.0	
Bleeding	141	34	455	9	14.9	44.1	**	17.1	100.0	**
Shock Evidence	14	8	150	3	28.6	75.0		0.7	33.3	*
Hepatomegaly	141	35	456	11	6.4	45.7	**	3.1	0.0	
Rash / Petechiae	13	8	145	3	61.5	75.0		50.3	33.3	
Abdominal Pain	141	35	458	11	20.6	54.3	**	20.5	45.5	
Dehydration	141	35	458	11	36.2	60.0	*	31.2	54.4	
Thrombocyptopenia_50	140	35	452	11	10.0	42.9	**	22.1	36.4	
Thrombocyptopenia_100	140	35	452	11	31.4	71.4	**	60.2	63.6	
Haemoconcentration_20	140	35	457	11	21.4	57.1	**	9.8	27.3	
Haemoconcentration_50	141	35	460	11	3.5	14.3	*	0.9	9.1	

[a] Pearson χ^2 test of independence for *Clinical Diagnosis_2* and symptom significant at * 5% or ** 1% with continuity correction.

Comparing the same set of symptoms between the adult and child patients separated by either DF or DHF classification, the results in Table 4.22 are obtained. For DF, symptoms that differed significantly between children and adults were muscle and joint pain, thrombocytopenia, shock, hepatomegaly and haemoconcentration, with the latter three more commonly observed in children. Again, due to the small sample size of certain categories, the percentages should be interpreted with caution.

Though diagnosed as DF, there were still some 35% of children and 0.7% of adults who exhibited shock syndrome. Seeing that, reconsideration should be given as they ought to be classified as the more critical DHF or DSS.

For those classified as DF, 1.9% of the children and 0.2% of adults displayed haemoconcentration_50 with hematocrit changes of 50% or higher. Such condition called for greater care and attention (than the conventional DF) as it indicated serious plasma leakage.

Some DF cases exhibited thrombocytopenia_100 (22.7% of child and 52.4% of adults) and hence should be treated as "DF with unusual haemorrhage" which according to WHO should be differentiated from the conventional DF without haemorrhage and the DHF (refer to Figure 1.2 in Chapter 1 for further illustration).

Among the DHF cases, more children recorded hepatomegaly and dehydration as shown in Table 4.22. Even though evidence of shock was shown to be more common in children, the significance could be due to the small sample size. Nonetheless, all children classified as DHF experienced shock and should be recognized as the more severe form of DHF (grade III or IV which are also termed DSS according to WHO grading guideline, as explained in Chapter 2).

Table 4.22: Percentage of clinical and laboratory findings for children and adults grouped by the diagnosis of DF and DHF as per the WHO guideline[b]

	No. of DF		No. of DHF		DF (%)			DHF (%)		
Symptom	Child	Adult	Child	Adult	Child	Adult	Sig.[a]	Child	Adult	Sig.[a]
Fever	160	485	40	43	92.5	93.6		92.5	90.7	
Vomit	155	484	37	43	47.1	49.0		78.4	69.8	
Giddiness	155	483	37	42	24.5	19.9		35.1	14.3	
Headache	17	137	3	29	35.3	46.7		33.3	48.3	
Skin Rash	20	139	3	30	70.0	51.1		66.7	40.0	
Eye Pain	19	140	3	29	10.5	17.1		0.0	13.8	
Muscle & Joint Pain	19	141	3	29	42.1	68.1	*	33.3	69.0	
Bleeding	154	479	37	40	17.5	16.5		27.0	40.0	
Shock Evidence	20	141	3	29	35.0	0.7	**	100.0	3.4	**
Hepatomegaly	155	480	37	42	11.6	3.3	**	27.0	4.8	*
Rash / Petechiae	19	135	3	29	57.9	49.6		100	44.8	
Abdominal Pain	155	482	37	42	24.5	18.5		43.2	38.1	
Dehydration	154	481	37	43	35.1	30.6		67.6	37.2	*
Thrombocyptopenia_50	154	479	37	42	3.2	16.9	**	62.2	64.3	
Thrombocyptopenia_100	154	479	37	42	22.7	52.4	**	100.0	100.0	
Haemoconcentration_20	160	485	40	43	10.0	2.3	**	100.0	100.0	
Haemoconcentration_50	160	485	40	43	1.9	0.2		17.5	14.0	

[a] Pearson χ^2 test of independence for *child or adult* and symptom significant at * 5% or ** 1% with continuity correction.

[b] Diagnosis of DHF is supported by laboratory findings of thrombocytopenia (platelet count <100,000/mm^3) and haemoconcentration (hematocrit changes > 20%).

The above analysis highlighted the differences between the various symptoms of DF and DHF (Table 4.20), as well as between the adult and child patients (Table 4.22) based on the proposed classification by WHO (1997a). Although a few symptoms such as shock, bleeding, hepatomegaly, abdominal pain, dehydration and vomiting were more frequent in those with DHF, there was no clear-cut or definite pattern that distinguished DHF from DF, save for thrombocytopenia and haemoconcentration which were artificially used to manipulate the classification of DF and DHF. Undoubtedly in this outbreak, more children manifested shock and hepatomegaly (Table 4.17), both of which were related to thrombocytopenia and haemoconcentration (WHO, 1997a).

4.10 Summary

More male patients were observed during the outbreak at the UMMC. In fact, there were more male then female in all the three main races. The suspected dengue patients who sought treatment at the UMMC were predominantly Malays. Age wise, most patients came from the working and schooling groups which may be attributed to the higher outdoor *Aedes* Index as reported by Tham (2001). The average age of these dengue patients was about 22 years. Children aged 12 and below constituted close to 30% of the dengue patient mix. More than 80% of all the cases were diagnosed as DF, while 5% being DHF and 1% DSS. The average length of stay was about 3.5 days for the admitted. The admission rate at UMMC for the dengue cases was 56.1%. Potential non-compliance was noted wherein 2.9% of the patients suffering thrombocytopenia of 50,000 platelet counts per mm^3 were not admitted though they should be as stipulated in the admission protocol. Of all the suspected dengue cases, only 62.3% of them were tested and confirmed serologically. About 65% of them who went for the test turned out positive. Close to half of the suspected dengue cases were not notified. In fact, the notification rate was about 54.5%. Such slack in the notification of the disease necessitates prompt consideration for improvement. In this study, greater proportion of children experienced shock, haemoconcentration, hepatomegaly, giddiness, abdominal pain and dehydration. Adults cited higher percentage of thrombocytopenia of 100,000 cells per mm^3 or less and muscle and joint pain. Potential inconsistencies in the clinical diagnosis of dengue infection based on the WHO guidelines suggests prospective room for improvement with regards to the proper classification of the dengue disease in order to improve the management of dengue patients at UMMC.