~ CHAPTER 7 ~

CONCLUSION

7.1 Overview

This chapter begins by summarizing the salient findings of this case study on the dengue patients at the University Malaya Medical Centre (UMMC) for the year 2002. The subsequent section presents some analytical discussions on the key findings and limitations of the study. The last part features a few thoughts and suggestions on the future study in this topic.

7.2 Summary of Findings

The three-and-a-half-month dengue episode at UMMC in year 2002 saw a higher ratio of male to female patients at about 13: 10. Such is the usual pattern observed at the national level as noted by Singh (2001), who found an almost equal distribution of male and female dengue patients throughout the country from 1992 to 1998.

Ethnicity wise, Malays made up the most (63%) followed by Chinese (18%) and Indian (16%). Albeit slightly different from the national level, this ethnic distribution could be the patient mix unique to UMMC.

About 30% of the dengue cases in this study were children aged 12 and below. Approximately 89% of the dengue patients aged 5 to 55 years. The figure implies that most dengue patients came from the working and school-going group. Such high

incidence in these two groups may correspond to the relatively higher outdoor *Aedes* Index in areas such as construction sites, schools, factories, rubbish dumpsites and children playgrounds as pointed by Tham (2001).

Admitted dengue cases spent an average of about 3.5 days for observation. Approximately 50% of them stayed for 2 to 4 days, regardless of whether they are children or adults.

The admission rate at the UMMC was 56.1% for this study. Children were more often admitted than adults. Contrary to the admission criteria, about 2.9% of those with thrombocytopenia of less than 50,000 per mm^3 were not admitted. Nevertheless, all of those with hematocrit changes of more than 50% were admitted in accordance to the said criteria. The non-compliance for the thrombocytopenia cases calls for additional study to understand the underlying cause.

Not all clinical dengue patients were tested serologically. Laboratory test was performed on about 62.3% of these patients. Of this, 65% of them were diagnosed positive of dengue infection. This percentage is higher than the national average of around 40.9% to 50.2% (proportion of laboratory confirmed dengue cases over total clinical cases) for the period of 1995 to 1999 (Singh, 2001).

Notification rate of the suspected dengue cases at the UMMC was quite low at only 54.5%. Close to half (45.5%) of these cases were not promptly notified as mandated by the disease control act.

Reclassification of the clinical DF and DHF cases by the WHO yardstick reveals potential non-conformity in the initial clinical diagnosis of dengue infection. There were 56 cases (54 clinical DF and 2 viral fever TRO DF) possibly over-diagnosed and 25 cases under-diagnosed (24 clinical DF and 1 DSS). This necessitates further investigation as to whether such non-conformity is deliberated.

Upon reclassification based on the WHO guidelines, it is observed that children diagnosed as having DHF had higher percentage of vomiting, shock, hepatomegaly, abdominal pain and dehydration, besides thrombocytopenia and haemoconcentration. Similarly, adult DHF cases also reported higher incidence of the same symptoms, except for shock, hepatomegaly and dehydration. Bleeding was frequently observed in adult DHF patients.

Comparing the adults and children in the DF category, it is noted that more adults suffered thrombocytopenia and muscle and joint pain, while higher proportion of children experienced shock, hepatomegaly and haemoconcentration. It should be noted that those cited evidence of shock, should be diagnosed provisionally as DHF (Grade III or IV) instead of the normal DF.

For the DHF category, there were more children who suffered shock, hepatomegaly and dehydration. Evidently, more children recorded shock syndrome and enlarged liver in this outbreak.

In predicting and classifying the outcome of the dengue serology test in this study, the constructed logistic model consists of three predictor variables, namely skin rash, abdominal pain and platelet count at admission. Although the model explains less than one fifth of the variation in the dengue serology test results, the classification accuracy was acceptable at 69% when compared to the chance-based criteria and the area under the ROC curve of 0.704 denote acceptable discrimination by the model. The logistic model with the three predictor variables essentially provides the differential diagnosis of positive dengue infection in the presence of other non-dengue viral diseases. Hence, patients suffering the said three symptoms should be tested serologically since more than half the time they might turn out positive.

In classifying the clinical diagnosis into DF and DHF, logistic modeling was performed separately for children and adults suspected of dengue. The expectation of the final logistic model is that it should capture both thrombocytopenia and haemoconcentration as they concurrently provides the diagnosis of DHF as per the definition by WHO. The final logistic model for children consists of five predictive variables – hepatomegaly, bleeding, abdominal pain, thrombocytopenia, and haemoconcentration – suggesting conformity to the WHO guidelines in the clinical diagnosis of pediatric patients. The classification accuracy of the model is proven better

than chance and the area under the ROC curve of 0.885 indicates excellent discrimination.

For the adults, the constructed logistic model contains only one predictive variable – hematocrit change – for the classification of clinical DF and DHF. The results suggest slack in keeping with the prescribed guidelines when diagnosing adult patients suspected of dengue infection. The model fails to capture the expected variable – thrombocytopenia – essential for establishing the diagnosis of DHF. Should the guidelines be consistently followed in the clinical diagnosis of adult DF/DHF, it is anticipated that the final model should contain at least one element that corresponds to platelet count (i.e. thrombocytopenia or platelet count at admission) and that thrombocytopenia should be significant in explaining DHF at the univariate level. Despite the high hit ratio, the classification accuracy of the model was deemed poor as shown by the area under the ROC curve of 0.592.

7.3 Discussion and Limitations of the Study

Numerous variables and cases in this study suffer a great deal of missing data causing them to be excluded in many analyses. These variables were listed in the chapter pertaining to data and methodology. As explained, the quality of the data is questionable where many of them assume irrational values and discretion has to be applied in removing these irregularities. It is not unreasonable to believe that the results of the analyses presented in this study are somewhat impaired and as such, interpretation must be done with great care.

More information such as fatality and follow-up with the non-admitted patients is needed to assess the adequacy of the current admission rate that may shed some lights on the efficiency and effectiveness of dengue patient management at UMMC.

The dengue notification rate at the UMMC should be looked into to understand if such low notification is due to failure to comply with the protocol or other reasons such as incorrect or missing data. It must be stressed that notification is strictly on clinical basis, and need not require laboratory confirmation. Attempt to understand the turnaround time of dengue notification at UMMC should be made to find out if there is significant delay which may lead to ineffective surveillance and control of further outbreak.

The effort of notification should be extended to included notification of laboratory confirmed dengue cases via serological and virological methods. Such active

surveillance will reflect any increased activity of the virus, location and time of the occurrence as well as disease severity (whether majority is DHF) which will aid in the control of outbreak (WHO, 1997b).

The findings in this study show that about two fifth of the probable dengue cases was not tested serologically for the virus. If the dengue serology test was not prescribed, was there other laboratory procedure performed (e.g. virological method such as virus isolation or detection of viral RNA)? If not, is the current prescription rate of dengue serology test acceptable? More study is required to answer these questions.

As demonstrated, the clinical diagnosis of DF/DHF among the adult patients suspected of dengue at the UMMC is questionable as to whether it is in accordance to the WHO guidelines. More study is required to further understand if such unconformity is due to special reasons and whether it has impaired the quality of treatment offered. It should be reminded that early recognition of DHF can significantly prevent shock and modify the severity of the disease.

All logistic models developed in this study will most likely fail outside the UMMC context due to different practice and patient mix. Nonetheless, this paper demonstrates that it is possible to derive a model that picks up factors significant in the differential diagnosis of dengue against other viral infections and allows the monitoring of these differential symptoms across time to observe changes. In addition, the paper also shows that the logistic technique makes it possible to gauge the level of compliance and

consistency in the clinical diagnosis of dengue infection in reference to the prescribed diagnostic guidelines.

Judging by the experience at the UMMC, this dengue outbreak is considered a mild one seeing that only 6.4% of the total cases were clinically diagnosed as DHF and DSS. If the WHO guidelines were applied, only about 11% of the cases in this episode would come under the more severe DHF and DSS definition, suggesting that this is more of a DF outbreak. Nevertheless, for the reason that many turned out positive of such infection (65% of those tested), this outbreak and any future DF outbreak for that matter should not be taken any less serious and diagnosis should be as accurate as possible to allow proper symptomatic treatment of the infection.

Should this be a DHF outbreak instead, it is likely that some if not many adult patients would be under-diagnosed, given the current inconsistency in the clinical diagnosis of adult DHF as shown in the paper. Such under-diagnosis, coupled with the low notification rate, might result in an underestimation of the momentum of a DHF outbreak.

7.4 Future Study

If a study were to be designed to include only serologically confirmed dengue patients and healthy subjects, the logistic model is then expected to capture all variables known to explain dengue infection. For such a design, further study on the interrelationship between the various clinical and laboratory symptoms is recommended so that similar symptoms can be factored and summarized together under the common dimensions using factor analysis to describe data in a much smaller number of concepts. For instance, skin rash, bleeding and platelet count can all be grouped under one dimension that measures haemorrhagic tendencies. Nonetheless, unlike this study, the constructed logistic model from a study that includes only the confirmed dengue cases and healthy subjects will very likely fail to differentiate dengue from other type of febrile illnesses that may mimic the features of dengue disease.

The quality of the dengue data collected in the future study can be improved via further planning, training and monitoring of all parties involved in the process of data collection possibly before the onset of any outbreak. When the data quality is improved, further meaningful analysis is made possible and the intangible cost associated with missing and unusable data can be minimized.