

**A RETROSPECTIVE STUDY ON FACTORS  
AFFECTING LENGTH OF STAY IN HOSPITAL  
UNIVERSITI SAINS MALAYSIA (HUSM) FOR  
DENGUE FEVER IN ADULT PATIENTS : A FIVE  
YEARS REVIEW**

**BY**

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Diperakui bahawa disertasi yg bertajuk **A RETROSPECTIVE STUDY ON FACTORS AFFECTING LENGTH OF STAY IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) FOR DENGUE FEVER IN ADULT PATIENTS : A FIVE YEARS REVIEW**

merupakan kerja dan penyelidikan yg asli dari **RAHAIZAH BINTI RANI**, nombor kad pengenalan: **810121-11-5272**, nombor matriks: **PUM 0385/11**, dari tempoh 2011 hingga 2016 adalah di bawah penyeliaan kami. Disertasi ini merupakan sebahagian daripada syarat untuk penganugerahan **Sarjana Perubatan Kecemasan**, segala hasil penyelidikan dan data yg diperolehi adalah hak milik terpelihara Universiti Sains Malaysia.

Tandatangan Pelajar

Tandatangan Penyelia Utama,  
Pensyarah Jabatan Kecemasan,  
Pusat Pengajian Sains Perubatan,  
Universiti Sains Malaysia.

Tandatangan Ketua Jabatan,  
Jabatan Kecemasan,  
Universiti Sains Malaysia.



# **ABSTRACT**

A RETROSPECTIVE STUDY ON FACTORS AFFECTING LENGTH OF STAY IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) FOR DENGUE FEVER IN ADULT PATIENTS : A FIVE YEARS REVIEW

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**Introduction** : Dengue fever is caused by dengue virus (DEN), a flaviviridae and transmitted to human by mosquito vector, usually *Aedes aegypti*. Basic clinical features recorded in adult dengue patients on admission to the emergency room are fever, headache, myalgia, back pain, arthralgia, vomiting, rashes, lymphocytopenia and thrombocytopenia. Dengue fever is a common presentation in emergency and trauma department in Malaysia and results in large number of hospital admission. However, there is no published data found regarding factors affecting length of stay in dengue fever especially in our country. Therefore this study was done to describe the socio-demographic, clinical profiles, outcome, length of stay and associated factors affecting length of stay.

**Objectives :** The aims of this study were to describe the statistic of dengue patients and their demographic characteristics, clinical profiles and its outcome and to determine mean length of stay in dengue patients. Besides, this study was done to determine the association between clinical profiles of dengue patients with dengue serology and to determine the association between socio-demographic characteristics and clinical profiles of dengue patients with length of stay. Apart from that, the other aim of this study was to identify associated factors in demographic characteristics and clinical profile of dengue patients affecting length of stay.

**Patients and Methods :** A retrospective cross-sectional study was done from January 2007 to December 2011 on eligible patients suspected or confirmed dengue fever in HUSM. Patients' medical records were traced from the record office, reviewed and the data were recorded using the data collection form. The socio-demographic characteristics, clinical profiles, outcome, length of stay, factors affecting length of stay and other parameters were analyzed using SPSS version 20.0.

**Results:** The mean age of the patients in this study was 33.95 (6.614) years old. 66.1% of patients were male, and the most common co-morbid diseases was hypertension (9.8%). All patients presented with fever, 95.3% had body ache and 58.8% had IgM positive. The mean length of stay was 3.98 (2.46) days. Symptom of rashes, diastolic blood pressure, shock index and haematocrit level were found to have significant association with dengue serology result. Patients with diabetes mellitus, hyperlipidaemia, symptom of rashes, pulse rate at emergency department, shock index in the ward, ascites and dengue serology result had significant association with length of stay. Patients with co-morbid diabetes mellitus,

background of hyperlipidaemia, underlying bronchial asthma, symptom of fever, diastolic blood pressure reading at emergency department, temperature at emergency department and ascites were the significant associated factors affecting length of stay.

**Conclusion:** We concluded that socio-demographic as well as clinical profiles were the associated factors affecting length of stay in dengue fever. Diabetes mellitus, hyperlipidaemia, bronchial asthma, symptom of fever, diastolic blood pressure at emergency department, temperature at emergency department, and ascites were the significant associated factors affecting length of stay in dengue patients.

**Dr Shaik Farid Abdull Wahab: Supervisor**

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# **LIST OF ABBREVIATIONS**

ANOVA	Analysis of Variance
APEX	Accelerated Programme for Excellent
CI	Confidence Interval
DBP	Diastolic Blood Pressure
ED	Emergency Department
Hb	Haemoglobin
Hct	Haematocrit
IgM	Immunoglobulin M
HUSM	Hospital Universiti Sains Malaysia
PR	Pulse Rate
SD	Standard deviation
SPSS	Statistical Package for Social Sciences
SBP	Systolic Blood Pressure
TWC	Total White Cell
WHO	World Health Organization

# **ABSTRAK**

## **KAJIAN RETROSPEKTIF TENTANG FAKTOR-FAKTOR MEMPENGARUHI TEMPOH KEMASUKAN KE WAD DI HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) BAGI DEMAM DENGGI DI KALANGAN PESAKIT DEWASA : KAJIAN LIMA TAHUN**

### **PENGENALAN**

Demam denggi disebabkan virus denggi flaviviridae dan dipindahkan kepada manusia oleh vektor, biasanya nyamuk *Aedes aegypti* atau *Aedes*. Kebiasaannya, ciri-ciri klinikal bagi pesakit demam denggi dewasa yang menerima rawatan di jabatan kecemasan adalah demam, sakit kepala, sakit-sakit otot, sakit belakang, sakit sendi, muntah, ruam-ruam, paras limfositopenia dan trombositopenia. Demam denggi adalah antara masalah yang sering ditemui di jabatan kecemasan dan menyebabkan kadar kemasukan ke wad yang tinggi. Walaubagaimanapun, data berkenaan faktor-faktor yang mempengaruhi tempoh kemasukan pesakit demam denggi ke wad tidak pernah diterbitkan, terutamanya di Malaysia. Justeru itu, kajian ini dibuat untuk mengkaji sosio-demografi, ciri-ciri klinikal, kesan, tempoh kemasukan ke wad serta faktor-faktor mempengaruhi tempoh kemasukan ke wad.



## **OBJEKTIF**

1. Untuk menentukan statistik demam denggi termasuk ciri-ciri sosio-demografi, ciri-ciri klinikal dan kesan-kesannya.
2. Untuk menentukan min bagi tempoh kemasukan ke wad bagi pesakit denggi.
3. Untuk menentukan kaitan antara ciri-ciri klinikal demam denggi dengan ujian serologi denggi.
4. Untuk menentukan kaitan antara ciri-ciri sosio-demografi, ciri-ciri klinikal demam denggi dengan tempoh kemasukan ke wad.
5. Untuk menentukan faktor-faktor sosio-demografi dan ciri-ciri klinikal yang menyumbang terhadap tempoh kemasukan ke wad bagi pesakit denggi.

## **METODOLOGI**

Satu kajian retrospektif telah dijalankan dari bulan Januari 2007 sehingga Disember 2011 ke atas pesakit demam denggi di HUSM. Rekod-rekod perubatan pesakit diperoleh dari pejabat rekod, dikaji dan maklumat direkodkan ke dalam borang maklumat kajian. Maklumat berkenaan ciri-ciri sosio-demografi, ciri-ciri klinikal, kesan, tempoh kemasukan ke wad, faktor-faktor yang memberi kesan terhadap tempoh kemasukan ke wad dianalisa menggunakan SPSS versi 20.

## **KEPUTUSAN**

Seramai 211 pesakit terlibat dengan kajian ini. Min bagi umur pesakit dalam kajian ini adalah 33.95 (6.614) tahun. 66.1% daripada pesakit adalah lelaki, dan penyakit kronik biasa ditemui di kalangan penghidap denggi adalah tekanan darah tinggi (9.8%). Didapati, semua pesakit mengalami simptom demam, 95.3% mengalami sakit-sakit badan, dan 58.8% pesakit adalah IgM positif. Min tempoh kemasukan ke wad adalah 3.98 (2.46) hari. Ruam, tekanan darah diastolik, indeks renjatan dan paras haematocrit mempunyai kaitan yang signifikan dengan keputusan ujian serologi denggi. Kencing manis, hiperlipidemia, ruam, kadar nadi di jabatan kecemasan, indeks renjatan di wad, ascitis dan serologi denggi mempunyai kaitan signifikan dengan tempoh kemasukan ke wad. Sementara itu, diabetes mellitus, hiperlipidemia, bronkial asthma, simptom demam, tekanan darah diastolik dan suhu badan di jabatan kecemasan serta ascites adalah faktor-faktor signifikan terhadap tempoh kemasukan ke wad.

## **KESIMPULAN**

Melalui kajian retrospektif ini, kami membuat kesimpulan bahawa sosio-demografi dan juga ciri-ciri klinikal adalah faktor-faktor yang mempengaruhi tempoh kemasukan ke wad bagi demam denggi. Sementara itu, diabetes mellitus, hiperlipidemia, 'bronchial asthma', demam, tekanan darah diastolic dan suhu badan di jabatan kecemasan serta ascites adalah faktor-faktor yang mempengaruhi tempoh kemasukan ke wad.

## **ABSTRACT**

**A RETROSPECTIVE STUDY ON FACTORS AFFECTING LENGTH OF STAY  
IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) FOR DENGUE  
FEVER IN ADULT PATIENTS : A FIVE YEARS REVIEW**

**INTRODUCTION**

Dengue fever is caused by dengue virus (DEN), a flaviviridae and transmitted to human by mosquito vector, usually *Aedes aegypti*. Basic clinical features recorded in adult dengue patients on admission to the emergency room are fever, headache, myalgia, back pain, arthralgia, vomiting, rashes, lymphocytopenia and thrombocytopenia. Dengue fever is a common presentation in emergency and trauma department in Malaysia and results in large number of hospital admission. However, there is no published data found regarding factors affecting length of stay in dengue fever especially in our country. Therefore this study was done to describe the socio-demographic, clinical profiles, outcome, length of stay and associated factors affecting length of stay.

**OBJECTIVES**

1. To describe the statistic of dengue patients and their demographic characteristics, clinical profiles and its outcome.
2. To determine mean length of stay in dengue patients.
3. To determine the association between clinical profiles of dengue patients with dengue serology
4. To determine the association between socio-demographic characteristics and clinical profiles of dengue patients with length of stay
5. To identify associated factors in demographic characteristics and clinical profile of dengue patients affecting length of stay

## **METHODOLOGY**

A retrospective cross-sectional study was done from January 2007 to December 2011 on eligible patients suspected or confirmed dengue fever in HUSM. Patients' medical records were traced from the record office, reviewed and the data were recorded using the data collection form. The socio-demographic characteristics, clinical profiles, outcome, length of stay, factors affecting length of stay and other parameters were analyzed using SPSS version 20.0.

## **RESULTS**

1. .The mean age of the patients in this study was 33.95 (6.614) years old. 66.1% of patients were male, and the most common co-morbid diseases was hypertension (9.8%). All patients presented with fever, 95.3% had body ache and 58.8% had IgM positive. The mean length of stay was 3.98 (2.46) days. Symptom of rashes, diastolic blood pressure, shock index and haematocrit level were found to have significant association with dengue serology result. Patients with diabetes mellitus, hyperlipidaemia, symptom of rashes, pulse rate at emergency department, shock index in the ward, ascites and dengue serology result had significant association with length of stay. Patients with co-morbid diabetes mellitus, background of hyperlipidaemia, underlying bronchial asthma, symptom of fever, diastolic blood pressure reading at emergency department, temperature at emergency department and ascites were the significant associated factors affecting length of stay.

## **CONCLUSION**

We concluded that socio-demographic as well as clinical profiles were the associated factors affecting length of stay in dengue fever. Diabetes mellitus, hyperlipidaemia, bronchial asthma, symptom of fever, diastolic blood pressure at emergency department, temperature at emergency department, and ascites were the significant associated factors affecting length of stay in dengue patients.



# 1. **INTRODUCTION**

Dengue fever is caused by dengue virus (DEN), a flaviviridae that belongs to the family Flaviviridae. There are four serotypes of DEN designated as DEN-1, DEN-2, DEN-3, and DEN-4. In Malaysia, there is no predominant serotype. Patient who was infected by one serotype will have lifelong immunity to that particular serotype only but not to other serotypes (Messer et al., 2012). The viruses are transmitted to human subjects by mosquito vector, usually *Aedes aegypti* or *Aedes albopictus*.

The dengue virus was first isolated in 1940 during World War II. Since then, the occurrence of dengue fever was increased all over the world. Dengue fever becomes one of important health problem since 1950 (Alexander N et al. 2011). It is an endemic disease in South East Asian. Dengue was first reported in Malaysia in 1950. In Malaysia, dengue fever cases show an increasing trend, year by year (Azami NAM et al. 2012). Those in the age group of 15 years and above noted to have higher incidence rate. Most of the dengue cases are from urban area.

The incubation period for dengue is 4 to 7 days. Patients with dengue fever may present as asymptomatic or symptomatic which ranging from mild febrile illness to severe form of illness with a changing of clinical, haematological and serological profiles according to the duration of illness.(Health, 2010)

Following the incubation period, there are 3 phases of dengue illness namely febrile, critical, and recovery phase. During febrile phase, patient developed acute onset

of high grade fever for 2 to 7 days which may associated with myalgia, arthralgia, headache, nausea and vomiting. Some patients may have haemorrhagic manifestation ranging from mild haemorrhagic manifestation to massive bleeding such as petechiae, mucosal membrane bleeding as well as gastrointestinal bleeding. From laboratory investigation, particularly full blood count, there is progressive reduction of total white cell count. (Health, 2010)

At the end of febrile phase usually day 3 of fever or around defervescence phase often between day 3 to day 5 of fever, the critical phase will be followed. During this phase, there is a rapid drop in body temperature. Some patients may have clinical manifestation of an increase in capillary permeability which results in plasma leakage. During this period, severe forms of plasma leakage may occur such as clinical fluid accumulation, altered conscious level, and may progress to profound shock and death if inadequate fluid therapy given. From laboratory investigations, haemoconcentration and thrombocytopenia are usually detected. Usually, it will be associated with leucopenia, coagulopathy, elevation of transaminases and hypoalbuminaemia.

After 24 to 48 hours of critical phase, recovery phase will take place. During this phase, plasma leakage stops and there is reabsorption of extravascular fluid. Clinically, the symptoms improves as well as haemodynamic status. Full blood count revealed stabilization of haematocrit level or drops further due to haemodilution as a result of reabsorption of extravascular fluid. There is recovery of white cell count followed by platelet count.



According to World Health Organization (WHO), the traditional classification of dengue is defined as follows : Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS) whereas the revised WHO classification consists of Dengue without Warning Signs, Dengue with Warning Signs and Severe Dengue. Since this study is a retrospective study, the traditional classification of dengue fever will be used.

Basic clinical features recorded in adult dengue patients on admission to the emergency room are fever, headache, myalgia, back pain, arthralgia, vomiting, anorexia, diarrhea, postural hypotension and rashes. Among haematological abnormalities, lymphocytopenia developed from day 1 to day 4 of illness. Thrombocytopenia were observed four to seven days after the onset of fever and resolved during the second week. (Thomas et al, 2010).

All over the world, dengue illness have caused significant morbidity as well as mortality. Dengue illness has important economic impacts because of the burden to hospitals to hospitals, work absenteeism and risk of mortality. (Carrasco et al., 2011).

Dengue fever is a common presentation in emergency and trauma department in Malaysia. Dengue epidemics are responsible for a great numbers of hospitalizations. The presentation may vary from mild illness to life threatening condition which can result in morbidity and mortality.

Dengue fever usually results in large number of hospital admission in most of the countries. In Singapore, dengue hospitalizations cost SGD\$6.77 million including losses

due to work absenteeism. (V.J. Lee et al, 2008). There are a few studies from other countries in which describe regarding clinical profiles and outcome of dengue fever, such as dengue severity and mortality.

Despite all that, no published data is found regarding dengue morbidity and factors affecting dengue morbidity especially in our region. The aim of our present study is to retrospectively determine the prevalence of dengue patients and their demographic characteristics, clinical profiles and its outcome. The second goal is to determine the association between demographic characteristics and clinical profiles of dengue patients and length of stay. Our hypothesis is that demographic characteristics and clinical profile are the factors associated with length of stay in dengue patients.

## **2. LITERATURE REVIEW**

### **2.1 History of Dengue**

Dengue fever was detected since 1779-1780 (Guzmán and Kouri, 2002) and becomes a major cause of morbidity worldwide. The incidence of dengue fever was noticed to have a significant increment since 1950s.

In America, the first dengue haemorrhagic fever epidemic occurred in Cuba in 1981, followed by another 24 other countries in that region subsequently. In south east asia region, an epidemic of dengue haemorrhagic fever occurred in Philippines in 1954. It was then spread to other south east asia countries such as Thailand, Vietnam Indonesian as well as to other Asian countries (Pinheiro and Corber, 1997).

In Malaysia, the first dengue case was recognized in 1902. Malaysia had the first dengue haemorrhagic fever outbreak in 1962. Since the first case of dengue in Malaysia had been reported, the illness remained endemic and the number of cases has been increased year by year (Lam, 1994). The incidence rate of dengue was 167.76 per 100 000 population with a mortality rate of 0.02 according to Malaysian Ministry of Health in 2008 (Azami et al., 2011)

## **2.2 Overview of dengue fever**

In Malaysia, the median age group of dengue patient was 53 (Azami et al., 2011) as compared in Mecca, most patients were adults with the median age of 26 (Khan et al., 2008). In Singapore, the median age of patients for dengue fever was 32 (Lee et al., 2008).

Previous studies from Saudi Arabia and Pakistan showed most of the dengue patients are male. (Khan et al., 2008) (Khan et al., 2007). In Malaysia, one study described 91.60% were positive for dengue IgG, where 90.17% females and 93.75% males. (Azami et al., 2011).

Study in Singapore also revealed most of the dengue patients were male (Lee et al., 2008). Ethnically, dengue seroprevalence were as follows: Malay, 91.75% ; Chinese, 91.37% ; Indian and others, 91.53% (Azami et al., 2011).

## **2.3 Pathophysiology of dengue fever**

There were a few hypothesis in pathophysiology of dengue fever.

### **1) Activation of complement system**

Major non-structural protein 1 (NS1) of dengue virus is the important trigger to complement activation, due to the binding of antibodies to NS1. Complement activation will result in local and systemic effect.

## 2) Transient autoimmunity

Dengue infection will produce antibodies that bind to human plasminogen and inhibit plasmin activity. Anti NS1 antibodies also cross react with platelet causing transient thrombocytopenia. These antibodies also stimulate overproduction of nitric oxide that cause cell damage.

## 3) Cross reactive T-cell response

T-cell mediated pathology contributes to cytolysis as well as inflammation leading to tissue damage. It also produce high concentration of pro and antiinflammatory cytokines. This phenomenon will cause increased vascular permeability causing plasma leakage into extravascular spaces. Due to fluid loss from intravascular, it results in hemoconcentration and hypovolaemia leading to shock. As a result, it will cause tissue hypoxia and metabolic acidosis (Halstead, 1965)

## **2.4 Clinical features and laboratory findings in dengue**

A study from Pakistan gastrointestinal symptoms such as vomiting (64%), abdominal pain (29.1%) and diarrhoea (26.7%), are the most frequent symptoms observed among dengue patients at the time of presentation. Body aches were found in 23.8% of the patients and 37.8% of patients had diffuse erythematous/ maculopapular rash over face, upper torso and/or lower limbs (Khan et al., 2007). A study from Mecca revealed the most common presentation was malaise, followed by musculoskeletal pain, fever, headache, nausea and vomiting. Skin rash was reported as uncommon presentation. (Khan et al., 2008)

From laboratory findings in dengue patients, dengue illness in Philippines showed that most of the patients had thrombocytopenia (mean 38.1), leukopenia (mean 2.90), haemoconcentration with mean highest haematocrit at 44.9%, prolonged partial thromboplastin time, elevated serum glutamate pyruvate transaminase and hypoalbuminaemia. (Bomasang and Suzara-Masaga, 2008). In Penang, Malaysia, most of the patients had hemoconcentration (mean 40.9), thrombocytopenia (mean 76.58), leukopenia (mean 3.98) and elevated alanine transaminase (Alam et al., 2010).

A study from India showed dengue virus-specific IgM Mu capture ELISA was positive in 85.1% of patients (Sharma et al., 1998). Another similar study from Philippine also revealed 81% had dengue antibody using IgM capture ELISA (Bomasang and Suzara-Masaga, 2008).

## **2.5 Factors Influencing Dengue Illness**

(Khan et al., 2008) described patient with clinical complications due to dengue fever had significantly lower platelet count and higher aspartate transaminase level on admission.

A study from Pakistan revealed a few factors significantly associated with disease severity in dengue patients which are male patients, positive history of abdominal pain, thrombocytopenia at presentation, monocytosis, lymphocytosis, neutropenia, raised alanine aminotransferase (ALT), raised aspartate transaminase (AST) and length of hospital stay in days (Khan et al., 2007).

Another study from India showed respiratory rate, platelet count, hematocrit and haemoglobin were significant predictors of outcome in dengue fever patients whereas tachypnoea, ecchymoses and shock were of significance in predicting the survival of patients with dengue illness (Sharma et al., 1998).

Following epidemic in Cuba in 1981, a few risk factors were identified in severe form of dengue illness : pre- existence of antibodies to dengue virus, paediatric age group, adult females, and patients with comorbidities namely bronchial asthma, sickle cell anaemia and diabetis mellitus (Kouri et al., 1989)

## **2.6 Outcome of Dengue Fever**

A study from Singapore revealed the threshold for dengue admission in Singapore is low with 83% of hospitalization rate. Median length of stay of the dengue patients in Singapore is 4 days (2-7 days). The study also described that hospital admissions due to dengue fever in Singapore cost SGD\$ 6.77 million. (Lee et al., 2008).

In UMMC, the cost per bed day for dengue admission was increasing from RM 636 in year 2005 to RM 927 in the year 2009 (Suaya et al., 2009). (Sabrina *et al.* 2006) mentioned about cost per bed day for 11 district hospitals in Malaysia ranging from RM 436.06 to RM 585.36.

Prolonged shock with a normal or low hematocrit at the time of shock was recognized as a risk factor that contribute to severe form of dengue illness particularly dengue haemorrhagic fever and dengue shock syndrome (Lum et al., 2002).

The deaths of dengue fever is mainly due to severe acute organ failure including signs of ventricular failure, massive hepatic cytolysis, respiratory failure and septic shock with multiple organ failure (Thomas et al., 2010b).

## **2.7 Management of dengue**

Basically, there is no specific treatment in dengue fever. Treatment in dengue fever is mainly supportive treatment. Fluid replacement is one of supportive treatment besides antipyretic agent (Teixeira and Barreto, 2009).

With regard to blood transfusion in dengue fever, there is no role of transfusion in mild bleeding. Meanwhile, blood transfusion, either fresh packed cells or fresh whole blood is indicated in patient with significant bleeding. A study from Delhi suggests that, patients with platelet count  $< 20,000/\text{cumm}$  and risk of bleeding require urgent platelet transfusion. However, patients with platelet count 21-40,000/cumm only require platelet transfusion once they have any haemorrhagic manifestations.



### **3. RESEARCH HYPOTHESIS AND OBJECTIVES**

#### **3.1 Research Hypothesis**

Demographic characteristics and clinical profile are the associated factors affecting length of stay in dengue patients

#### **3.2 General research objective**

To describe socio-demographic characteristics, clinical profiles, outcome, length of stay and factors affecting length of stay in patients with dengue fever

#### **3.3 Specific objectives**

1. To describe the statistic of dengue patients and their demographic characteristics, clinical profiles and its outcome.
2. To determine mean length of stay in dengue patients.
3. To determine the association between clinical profiles of dengue patients with dengue serology
4. To determine the association between demographic characteristics and clinical profiles of dengue patients with length of stay
5. To identify associated factors in demographic characteristics and clinical profile of dengue patients affecting length of stay

## **4. METHODOLOGY**

### **4.1 Study Design and Duration**

This study was a retrospective study (retrospective record review) of a five years period from January 2007 till December 2011. The primary endpoint of the study was to determine the associated factors affecting length of stay in dengue patients.

### **4.2 Study Location**

This study was conducted at the Emergency Department, Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan which was a regional tertiary centre. Hospital Universiti Sains Malaysia also is a teaching institution dedicated to undergraduate and postgraduate training including Emergency Medicine. HUSM is the first university in Malaysia, granted as Accelerated Programme for Excellent (APEX). In order to achieve the target as one of the best university for medical research, there will be a lot of challenges waiting.

### **4.3 Study Approval**

This study was undertaken as a dissertation study for the Degree of Master of Medicine (Emergency Medicine) under the Hospital Universiti Sains Malaysia and approved by the department board review and hospital ethics committee on the 30<sup>th</sup> October 2013 (reference USMKK/PPP/JEPeM [268.4(1.4)]).

#### **4.4 Selection of Subjects**

The reference population were all patients diagnosed with dengue fever presented to hospitals in state of Kelantan. The source population were all patients diagnosed with dengue fever presented to Emergency Department, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan from January 2007 to December 2011. The eligible population were the source population fulfilling the inclusion and exclusion criteria. The study population consisted patients diagnosed with dengue fever presented to Emergency Department, Hospital Universiti Sains Malaysia during the study period.

##### **4.4.1 Inclusion criteria**

1. Patient suspected and confirmed (notifiable) with dengue based on WHO criteria presented to the Emergency Department at the time of study.

##### **4.4.2 Exclusion criteria**

1. Patient's age less than 18 years old

#### **4.5 Mode of data collection**

All patients presented with suspected or confirmed dengue fever, then admitted to the ward during the period from January 2007 to December 2011, were screened from the Emergency Department's attendance registry. Patients' medical records were traced from the record office based on their names and reference numbers. All available medical record folders were reviewed by the author personally and the data that were relevant were sought and recorded using the data collection form. An approval for tracing and using the data from patients' medical records has been granted from the

Director of HUSM on the 16<sup>th</sup> March 2014 (reference number: HUSM/11/020/Jld 6)  
(Appendix B).

#### 4.6 Sample size

Sample size was calculated using the single proportion formula. Prevalence of dengue fever occurs in about 91.6% of population (Muhammad Azami et al 2011).

The following formula was used:

$$\text{Sample size, } n = \left( \frac{z}{\Delta} \right)^2 p(1 - p)$$

$z$  = Z statistic for level of confidence

$p$  = expected prevalence

$\Delta$  = precision

Taking the  $z$  score as 1.96, expected prevalence of dengue fever at 91.6%, based on available literature and precision of 0.05, the sample size is calculated to be 118.

$$n = 118 + 10\% \text{ dropout rate} = 118 + 11.8 = 129.8 \approx 130$$

Retrospective sampling was done involving all cases of dengue fever.

#### **4.7 Assessment Form**

A data collection form written in English (**Appendix A**) was used in this study. It consisted of 6 components; (1) the demographic data, (2) symptoms during presentation, (3) physical examination, (4) diagnosis, (5) laboratory investigation results and (6) outcome.

The demographic data consists of age, gender, race, pre-morbid disease. Symptoms during presentation are fever, body ache, lethargy, nausea, vomiting, bleeding tendencies, rashes and abdominal pain. Physical examination parameters are general condition, systolic and diastolic blood pressure, pulse rate, Hess test, cardiovascular, respiratory, and abdominal examinations finding.

The third component of the assessment form is the diagnosis of the patients namely dengue fever, dengue haemorrhagic fever and dengue shock syndrome. In laboratory results, we studied on full blood count and dengue serology (Immunoglobulin M). Parameters of full blood count included total white count, haemoglobin level, haematocrit and platelet count. Another component was outcome of the study which comprises of length of stay, blood transfusion and 30-day mortality.

#### **4.8 Plans for minimizing result error**

The following steps were taken to reduce the error while conducting the study:

1. Patients were selected strictly according to the inclusion and exclusion criteria for this dengue fever study.
2. Any data that not recorded, not found or missing in patient medical record were excluded from the study.

#### **4.9 Data Analysis**

All data including the socio-demographic characteristics, clinical profiles, outcome, length of stay, factors affecting length of stay were analysed with Statistical Package for Social Sciences (SPSS) software version 20.0. Numerical variables were checked for normality and presented as mean and standard deviation or median where appropriate. Descriptive analysis was expressed as frequencies, percentages and presented as bar chart, pie chart, or line graphs as seen appropriate. Statistical significance was calculated between groups using independent t-test for continuous variables and Pearson chi-square test or Fisher's Exact test for categorical variables. A p value < 0.05 was considered as statistically significant for all statistical analysis in this study. The numerical variables in this study are:

1. Age
2. Systolic blood pressure
3. Heart rate
4. Respiratory rate
5. Mean arterial pressure
6. Oxygen saturation
7. Total white cell count
8. Hematocrit
9. Haemoglobin
10. Platelet

The categorical variables are:

1. Gender
2. Race
3. Dengue serology
4. Symptoms

To answer the objectives of this study, the data were analyzed in the following methods:

#### **4.9.1 Objective 1**

Numerical variables were checked for normality and presented as mean and standard deviation or median where appropriate. Categorical variables were expressed as frequencies, percentages and presented as bar chart, pie chart, or line graphs as seen appropriate.

#### **4.9.2 Objective 2**

Length of stay for dengue patients was expressed as mean and standard deviation or median.

#### **4.9.3 Objective 3**

The **Pearson's Chi-Square ( $\chi^2$ ) test** was used to assess the association between dengue serology result and different variables of clinical profiles. *P* value of less than 0.05 will be taken as statistically significant at 95% confidence interval (CI).

Variables involved are:

Dependent variable: Dengue serology (Negative/Positive).

Independent variable: Variables of clinical profiles (Yes/No)

#### **4.9.4 Objective 4**

**Independent t-test** (if independent variables have 2 groups) and **one-way ANOVA** (if independent variables >2 groups) were used to assess association between

socio-demographic and clinical profiles with length of stay. *P* value of less than 0.05 will be taken as statistically significant at 95% confidence interval.

Variables involved are:

Dependent variable: Length of stay (mean  $\pm$  s.d)

Independent variable: Variables of socio-demographic and clinical profiles

#### **4.9.5 Objective 5**

**Simple** and **multiple linear regression** analysis with forward stepwise method were used to identify the associated factors affecting length of stay. Predicting factors from univariate with p-value of  $\leq 0.05$  were incorporated into a multiple logistic regression analysis.



## **4.10 Definition of Terms**

### **4.10.1 Probable/Suspected Dengue**

Live in/ travel to dengue endemic area.

- Fever and 2 of the following criteria:
- Nausea, vomiting
- Rash
- Aches and pains
- Torniquet test positive
- Leukopenia
- Any warning sign

### **4.10.2 Warning Signs**

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargement > 2cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

### **4.10.3 Dengue Fever**

Acute febrile illness with two or more of the following :

- Headache
- Retroorbital pain
- Myalgia
- Leukopenia
- Arthralgia
- Rash
- Haemorrhagic manifestation
- Supportive serology occurrence at the same location and time as other confirmed cases of dengue fever

### **4.10.4 Dengue Haemorrhagic Fever**

All of the following must be present:

- Fever or history of acute fever, lasting 2-7 days, occasionally biphasic
- Haemorrhagic manifestation
  - Positive tourniquet test
  - Petechia, purpura or bleeding from mucosa, gastrointestinal tract, injection sites or other locations; or
  - Haematemesis/melena
- Thrombocytopenia ( $<100\,000$  platelets per  $\text{mm}^3$ )
- Evidence of plasma leakage due to increased vascular permeability

#### **4.10.5 Dengue Shock Syndrome**

Dengue Haemorrhagic Fever with hypotension for age or narrow pulse pressure (<20 mmHg), plus one of the following:

- Rapid and weak pulse
- Cold, clammy skin, restlessness

#### **4.10.6 Length of Stay**

The number of days of care counted from the admission date to the separation (discharge) date for patients within a healthcare facility (Fransoo et al. 2013)

#### **4.10.7 Systolic blood pressure**

Maximum arterial pressure during systole. It can be classified into :

- Normal range : 90-140 mmHg
- Hypertension : > 140 mmHg
- Hypotension : < 90 mmHg (Robert and Jerris, 2014)

#### **4.10.8 Diastolic blood pressure**

Minimum arterial pressure during diastole and occurs just before the onset of ventricular ejection. It can be classified into :

- Normal range : 60-90 mmHg
- Hypotension : <60
- Hypertension : >90 (Robert and Jerris, 2014)

#### **4.10.9 Shock index**

Related to left ventricular stroke work in acute circulatory failure.

Calculation : Heart rate/systolic blood pressure.

It can be classified into :

- Normal range : 0.5 – 0.7
- Low : < 0.5
- High : > 0.7 (Mahadevan & Gus, 2012)

#### **4.10.10 Pulse rate**

It can be classified into

- Normal range : 60-100 beats per minute
- Bradycardia : < 60beats per minute
- Tachycardia : > 100 beats per minute (Andrew, 2012)

#### **4.10.11 Total white count**

It can be classified into

- Normal range : 4 000 – 11 000/  $\mu$ L
- Low : < 4000/  $\mu$ L
- High : > 11 000/  $\mu$ L (Stephen & Gary, 2009)

#### **4.10.12 Physical findings**

- Emergency department :first physical examination done at emergency department
- Ward : first physical examination done in the ward

#### **4.10.12 Hess test**

- Test is done by inflating a blood pressure cuff on the upper aspect of arm to a point midway between systolic and diastolic pressure for 10 minutes.
- Positive if  $> 20$  petechiae/ $2.5 \text{ cm}^2$  are observed. (Emy *et al.*2010).

#### 4.11 Flow chart of the study

