

**FACTORS RELATED TO SHOCK AMONG DENGUE PATIENTS  
IN KHON KAEN HOSPITAL, THAILAND**

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**A THESIS SUBMITTED IN PARTIAL FULFILLMENT  
OF THE REQUIREMENTS FOR  
THE DEGREE OF MASTER OF SCIENCE (PUBLIC HEALTH)  
MAJOR IN INFECTIOUS DISEASES AND EPIDEMIOLOGY  
FACULTY OF GRAGUATE STUDIES  
MAHIDOL UNIVERSITY  
2008**

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Thesis  
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IN KHON KAEN HOSPITAL, THAILAND**

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was submitted to the Faculty of Graduate Studies, Mahidol University  
For the degree of Master of Science (Public Health)  
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## **ACKNOWLEDGEMENTS**

I would like to express my sincere gratitude and deep appreciation to my major advisor, Associate Professor Kulaya Narksawat for her invaluable supervision, guidance, constructive criticism, and tremendous assistance throughout my study. She has never lacked in kindness and support.

My gratefulness and deepest appreciation is given to my co-advisor, Assistant Professor Sukhum Jiamton and Assistant Professor Sukhontha Kongsin for their invaluable advice, improving this thesis and for helpful guidance to the statistical analysis of the data.

It is impossible to mention all the kindness and helpfulness of lectures, and staff of Epidemiology Department for their helps that made this study possible.

I wish to thank Mr. Arthit Limpaisarn and my friends in research team for their helpful advices to the successful completion of this thesis.

My special thank to all physicians, nurses and staffs of pediatric ward, pediatric intensive care unit, medical ward and statistical unit, Khon Kaen Hospital for their cooperation.

I am particularly indebted to the Faculty of Graduate Studies, Mahidol University for the scholarship, which enabled me to undertake this study.

Finally, I would like to express my deep appreciation to my parents and my sister who continuously provided unlimited moral support throughout the study period and for their willingness to sacrifice during a long period away from them.

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**FACTORS RELATED TO SHOCK AMONG DENGUE PATIENTS IN KHON KAEN HOSPITAL, THAILAND**

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**ABSTRACT**

A hospital-based case-control study was conducted to assess factors related to Dengue Shock Syndrome (DSS) among patients with dengue admitted in Khon Kaen Hospital from 2<sup>nd</sup> June, 2007 to 2<sup>nd</sup> November, 2007. Data collection was performed by interviewing and analysis of medical records. Regarding clinical status at discharge, 37(17.2%) and 178(82.8%) of 215 patients were respectively diagnosed with DSS (=Case) and without DSS (=Control).

The sex ratio (male : female) was 1.3 : 1 in DSS group vs. 0.98 : 1 in non DSS group. The mean (SD) age of DSS group and non DSS group was 9.3 (4.3) years and 12(5.5) years, respectively. Nearly all DSS patients and about fourth percent of the non DSS group lived in a rural areas ( $p < 0.001$ ). Most DSS patients and one-third of the non DSS group were referred cases ( $p < 0.001$ ). More than half of the DSS group reported that they had a reduction of urine output, muscle or joint pain, bleeding and diarrhea before admission. During admission, all patients in the DSS group had clinical evidence of plasma leak and most of them had anorexia and epigastric pain. Half of the patients in DSS group had pleural effusion and abdominal pain. Two-fifths of this group had ascites and enlargement of liver.

Results from unconditional logistic regression analysis demonstrated significant clinical, demographic and socio-economic factors related to DSS. Significant clinical symptoms before admission were bleeding (adjusted OR = 12.00, 95%CI: 3.15–45.44) and not having muscle pain or joint pain (adjusted OR = 6.77, 95%CI: 1.83–25.00). Significant clinical signs during admission were negative tourniquet test (adjusted OR = 5.52, 95%CI: 1.52–20.13), enlargement of liver (adjusted OR = 3.76, 95%CI: 1.15–12.32) and ascites during admission (adjusted OR = 7.83, 95%CI: 2.16–28.37). Significant demographic and socio-economic factors were being male (adjusted OR = 7.93, 95%CI: 2.02–31.10) and living in a rural area (adjusted OR = 42.21, 95%CI: 4.92–362.32).

This study suggests possible clinical signs and symptoms associated to shock syndrome among dengue patients and might provide good guidance for close monitoring for prompt and adequate fluid replacement therapy to prevent the progression in severity of this disease.

**KEY WORDS: DENGUE SHOCK SYNDROME / FACTORS / DENGUE PATIENTS**

ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกเดงกีที่มารับการรักษาพยาบาลในโรงพยาบาลขอนแก่น ประเทศไทย (FACTORS RELATED TO SHOCK AMONG DENGUE PATIENTS IN KHON KAEN HOSPITAL, THAILAND)

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#### บทคัดย่อ

การศึกษานี้เป็นการศึกษาแบบ Hospital-based case-control study ทำการศึกษาผู้ป่วยไข้เลือดออกเดงกีที่มารับการรักษาที่โรงพยาบาลขอนแก่น ประเทศไทย ระหว่างวันที่ 2 มิถุนายน 2550 ถึง 2 ตุลาคม 2550 เป็นเวลา 5 เดือน เพื่อศึกษาปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกเดงกีที่มารับการรักษาพยาบาลในโรงพยาบาลขอนแก่น วิธีการเก็บรวบรวมข้อมูล คือการสัมภาษณ์ผู้ป่วยและญาติผู้ดูแลผู้ป่วยและการคัดลอกข้อมูลลักษณะอาการทางคลินิกจากแฟ้มประวัติผู้ป่วย กลุ่มที่ทำการศึกษาทั้งหมด 215 ราย ประกอบด้วย กลุ่มศึกษา คือ ผู้ป่วยที่ช็อก จำนวน 37 ราย (ร้อยละ 17.2) และกลุ่มเปรียบเทียบ คือ ผู้ป่วยที่ไม่ช็อก จำนวน 178 ราย (ร้อยละ 82.8)

สัดส่วนเพศชายต่อเพศหญิงในกลุ่มศึกษา คือ 1.31 : 1 และในกลุ่มเปรียบเทียบ คือ 0.98 : 1 ค่าเฉลี่ย (SD) ของอายุในกลุ่มศึกษา เท่ากับ 9.3(4.3) และกลุ่มเปรียบเทียบ เท่ากับ 12(5.5) ส่วนใหญ่ในกลุ่มศึกษาและประมาณร้อยละ 40 ในกลุ่มเปรียบเทียบคือผู้ป่วยที่อาศัยในเขตชนบท ( $p < 0.001$ ) ส่วนใหญ่ในกลุ่มศึกษาและหนึ่งในสามในกลุ่มเปรียบเทียบ คือผู้ป่วยที่ได้รับการส่งต่อจากโรงพยาบาลอื่น ( $p < 0.001$ ) อาการทางคลินิกก่อนมารับการรักษาในโรงพยาบาลพบว่า มากกว่าครึ่งหนึ่งในกลุ่มศึกษา มีอาการปัสสาวะออกน้อย ปวดกล้ามเนื้อหรือปวดตามข้อและมีเลือดออก อาการทางคลินิกระหว่างรับการรักษาในโรงพยาบาล คือ กลุ่มศึกษาทุกคนมีอาการแสดงการรั่วของน้ำในเซลล์ ส่วนใหญ่มีอาการเบื่ออาหารและปวดท้อง โดยครึ่งหนึ่งในกลุ่มนี้มีอาการน้ำในช่องเยื่อหุ้มปอดและมีอาการปวดท้องและสองในห้าในกลุ่มดังกล่าวมีอาการน้ำในช่องท้องและมีภาวะตับโต

ผลการศึกษาวิเคราะห์โดยใช้ Unconditional logistic regression ด้วยวิธี Enter เพื่อหาความสัมพันธ์ระหว่างปัจจัยที่เสี่ยงทางด้านอาการต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกเดงกี โดยควบคุมตัวแปรที่มีอิทธิพลต่อการเกิดการช็อกอื่น ๆ พบการมีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติของ อาการทางคลินิกก่อนมารับการรักษาในโรงพยาบาล ได้แก่ การมีเลือดออก (adjusted OR = 12.00, 95%CI = 3.15 – 45.44) และการไม่มีอาการปวดกล้ามเนื้อปวดข้อ (adjusted OR = 6.77, 95%CI = 1.83 – 25.00) และ อาการทางคลินิกระหว่างการรับรักษาพยาบาลในโรงพยาบาลขอนแก่น ผลการทดสอบทูนิเกตต์ เทสต์เป็นลบ (adjusted OR = 5.52, 95%CI = 1.52 – 20.13) การมีภาวะตับโต (adjusted OR = 3.76, 95%CI = 1.15 – 12.32) และการมีน้ำในช่องท้อง (adjusted OR = 7.83, 95% CI = 2.16 – 28.37) ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกเดงกี ด้านประชากรและเศรษฐกิจสังคม ได้แก่ ได้แก่ เพศชาย (adjusted OR = 7.93, 95%CI = 2.02 – 31.10) และอาศัยอยู่ในเขตชนบท (adjusted OR = 42.21, 95%CI = 4.92 – 362.32)

จากการศึกษานี้แสดงถึงอาการช้ำน้ำและปัจจัยที่ทำให้ผู้ป่วยไข้เลือดออกมีความเสี่ยงต่อการเกิดภาวะภาวะช็อกในผู้ป่วยไข้เลือดออกเดงกี โดยมีข้อเสนอแนะจากผลการศึกษานี้คือ ผู้ป่วยไข้เลือดออกที่มีปัจจัยเสี่ยงเหล่านี้ ควรได้รับการสังเกตอาการแสดงเริ่มแรกของภาวะช็อกอย่างใกล้ชิด เนื่องจากการให้สารน้ำทดแทนอย่างเพียงพอในทันทีสามารถป้องกันการเกิดการช็อกได้

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## **CHAPTER 1**

### **INTRODUCTION**

#### **1.1 Rationale and Justification**

##### **The global burden of dengue viral infection**

At the present time, Dengue Fever (DF) and Dengue Haemorrhagic Fever (DHF) are the most important arthropod - borne virus diseases of public health significance among other infectious diseases. Comparing among nine reporting countries in the 1950s, by geographic distribution, DH and DHF occurred in more than 100 countries worldwide. The World Health organization (WHO) estimated that more than 2.5 billion people were at risk of dengue infection (1).

Dengue fever (DF), Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) are caused by Dengue virus (single stranded RNA virus in Family *Flavivirida*) divided into 4 serotypes (DEN 1, DEN 2, DEN 3, DEN 4) (2). The four viral serotypes are transmitted from viraemic to susceptible humans mainly by bites of *Aedes aegypti* and *Aedes albopictus* mosquito species (3).

Dengue is divided into 3 symptom-groups (Dengue Fever, Dengue Haemorrhagic Fever and Dengue shock syndrome). Dengue fever always is in adolescent and adult. Some case of dengue fever is not severe. The common symptom is fever, headache, retroocular pain accentuated by eye movements, backache and pain in the muscles. Arthralgias may be severe, which is why dengue fever was also known as break bone fever. These symptoms vary in severity and usually persist for several days. The high index of suspicion based on period, population & place and absence of convincing evidence of any other febrile illness (3-6)

Dengue Haemorrhagic Fever is characterized by high fever, haemorrhagic phenomena, hepatomegaly, and often circulatory failure. Moderate to marked thrombocytopenia with concurrent haemoconcentration are distinctive clinical laboratory

findings. The major pathophysiological change that determines the severity of disease in DHF – and differentiates it from DF- is the leakage of plasma, as manifested by an elevated haematocrit (i.e. haemoconcentration), a serous effusion or hypoproteinaemia (3).

Dengue Shock syndrome has evidence of plasma leakage and shown by 20% in haematocrit, hepatomegaly, pleural effusion, ascites, cold perspiration, severe liver involvement and right – upper quarter abdominal tenderness and confusion (7-9). The other symptom was manifestations of respiratory difficulty, melena, haematemesis, cold clammy skin, narrow pulse, pressure, prolong capillary refill, shock, tachycardia, coma and tourniquet test. The hypotension for age, cold clammy skin, restlessness, rapid weak pulse, narrow pulse pressure ( $\leq$  mm of Hg) and profound shock (10).

The dengue is endemic in all WHO Regions except the European Region (EUR). The major dengue burden was found in South-East Asia and the western Pacific, with increased reporting of DF/DHF in the Americas. WHO reports found that 2.5 billion people (living in the tropics and sub tropics) are at risk of DF/DHF, and that 1.3 billion live in South–East Asia Region. Eight countries in these Regions (Bangladesh, India, Indonesia, Maldives, Myanmar, Sri Lanka, Thailand and Timor-Leste) have reported disease incidence every year. Outbreak was reported for the first time in Bhutan in 2004. Nepal and Korea have never reported any case of DF/DHF (3).

The economic impact of dengue was studied in many countries. The cost of the 1981 Cuban epidemic of DHF/DSS was estimated to be approximately US\$103 million (11). Another example was DF and DHF/DSS epidemic in Puerto Rico since 1977 which was estimated to have cost US\$150 – 200 million (12). A 1995 report estimated that the annual economic burden due to DHF in Thailand ranged from US\$19 million to US\$51 million per year, depending on whether low or high levels of transmission occur (13).

### **DF/DHF/DSS in Thailand**

The first epidemic outbreak occurred in 2001 with 2,158 cases of dengue patients, a morbidity rate of 8.80/100,000 pop and a mortality rate of 13.90% (14). Every year at the beginning of February, there was a gradual starting of increase in the incidence of DHF cases, peaks in July and August, with the monthly number of cases declining thereafter. There were four serotypes of dengue circulating in Thailand the

proportion of each serotype varies from year to year (15-19). The trend of the incidence of the disease had continued to increase in a cyclic pattern. The disease mainly affected the younger age-groups of less than 15 years with the highest proportion of cases occurring in the age group 5-9 years, followed by the age group 10-14 years (20). Two to three years later dengue had started to appear among patients whose age was above 15 years. The highest age of dengue patients reported among adults was 72 years old. As such, physicians now gave importance to adult patients. Some dengue patients who were older than 15 years old died in 2002 (2).

### **DF/DHF/DSS situation in Khon Kaen province**

In 2005, it was found that the number of cases of dengue slightly increased when compared to 2004. There were 746 cases of dengue with morbidity rate of 42.83 per 100,000 population, and 3 deaths with mortality rate of 0.4 %. The distribution of dengue in Khon Kaen province was similar to country level. There was a gradual starting of increase in the incidence of dengue cases, peak in July and August (21).

### **Khon Kaen Hospital**

Khon Kaen Hospital was a regional hospital with 867 beds and 111 units of administration under the Division of Regional Hospital, Ministry of Public Health. Health services provided for the population in Khan Kaen province and population of other provinces nearby were at every level of care: primary, secondary and tertiary care. The average number of out patients was 7,828 per month and in patients were 4,912 per month (22).

The number of dengue cases during 2002-2006 from the reports demonstrated a decrease from 1,828 cases in 2002 to 488, 325 and 380 cases in 2003, 2004 and 2005 respectively. The number of dengue shock syndrome (DSS) also decreased from 291 cases in 2002 to 78, 49 and 89 in 2003, 2004 and 2005 respectively. The distribution of dengue cases in Khon Kaen Hospital increased every two or three years (22).

Dengue was an important global disease and Thailand was a dengue endemic area. The disease hit every age - group and every region in Thailand. Morbidity of dengue was not specific to children groups but was now increasing among adult patients. Some dengue patients older than 15 years old died in 2002 because they were diagnosed

by a physician not interested in adult dengue patients (15-19). Severe cases in dengue patients might have shock from leak of plasma causing them to die instantly because there was not a right diagnosis and treatment (2, 4). At present there was no drug that could kill Dengue virus and Dengue vaccine still had not been successes. From the dengue situation, which was a public health problem and the patients with severe dengue could die, the patients with DSS must be promptly treated to mitigate the symptoms as well as to better manage and prevent the patients with dengue from shock. Dengue Shock Syndrome had an impact physically, mentally and economically on the patients and household. So in this study the Researcher was interested in the factors related to shock with dengue. This would be useful for patients and people to prevent the development of shock and for Public Health authorities in designing proper management and preventive intervention of Dengue Shock Syndrome that caused death and mortality in people.

## **1.2 Research Question**

What were the factors related to shock among dengue patients admitted to Khon Kaen Hospital during June to November in 2007?

## **1.3 Research Objective**

### 1.3.1 General Objective

To assess factors associated with shock among dengue patients admitted to Khon Kaen Hospital.

### 1.3.2 Specific Objectives

1. To assess the associations between clinical symptoms before admission, which were history of illness with dengue before, history of underlying diseases, duration of fever before admission, bleeding and shock among dengue patients admitted to Khon Kaen Hospital.

2. To assess the associations between clinical signs and symptoms during admission which were duration of fever during admission, plasma leakage,

positive TT, enlargement of liver, laboratory results as increasing of haematocrit, low of platelet counts and shock among dengue patients admitted to Khon Kaen Hospital.

3. To assess the associations between demographic variables of dengue patients and caregivers, which were age of patients and caregivers, sex of patients and caregivers, body size, BMI of patients and shock among dengue patients admitted to Khon Kaen Hospital.

4. To assess the associations between socio-economic status of patients and caregivers, which were education of patients, household's income of caregivers, household's expenditure of caregivers, occupation of patients and caregivers, residency (urban or rural) and shock among dengue patients admitted to Khon Kaen Hospital.

## **1.4 Hypothesis**

There were associations between Dengue Shock Syndrome (DSS) among dengue patients admitted to Khon Kaen Hospital and factors associated were:

### 1.4.1 Clinical sign symptoms:

- 1) History of illness with dengue before and history of underlying diseases.
- 2) Clinical symptoms before admission which were duration of fever before hospitalization and bleeding.
- 3) Clinical data during admission: Signs and symptoms such as plasma leakage, positive TT and enlargement of liver.
- 4) Laboratory finding such as increasing of haematocrit and low of platelet counts.

1.4.2 Demographic variables: Age of patients and caregivers, sex of patients and caregivers, including body size and BMI of patients.

1.4.3 Socio-economic variables: Education of patients and caregivers, household's income, household's expenditure, occupation of patients and caregivers, and residency (urban or rural) of patients.

## **1.5 Scope of the Study**

Hospital based case-control among dengue patients admitted for treatment in Khon Kaen Hospital was conducted during June to November in 2007. Cases with Dengue Shock Syndrome (DSS) were collected at the time of admission and collected during the period of time of study. Data on factors related to DSS and factors related to shock among dengue patients were explored by interviewing and retrieving information from medical records. Such factors were demographic characteristics, socio-economic characteristics and clinical signs and symptoms and laboratory results.

## **1.6 Benefit**

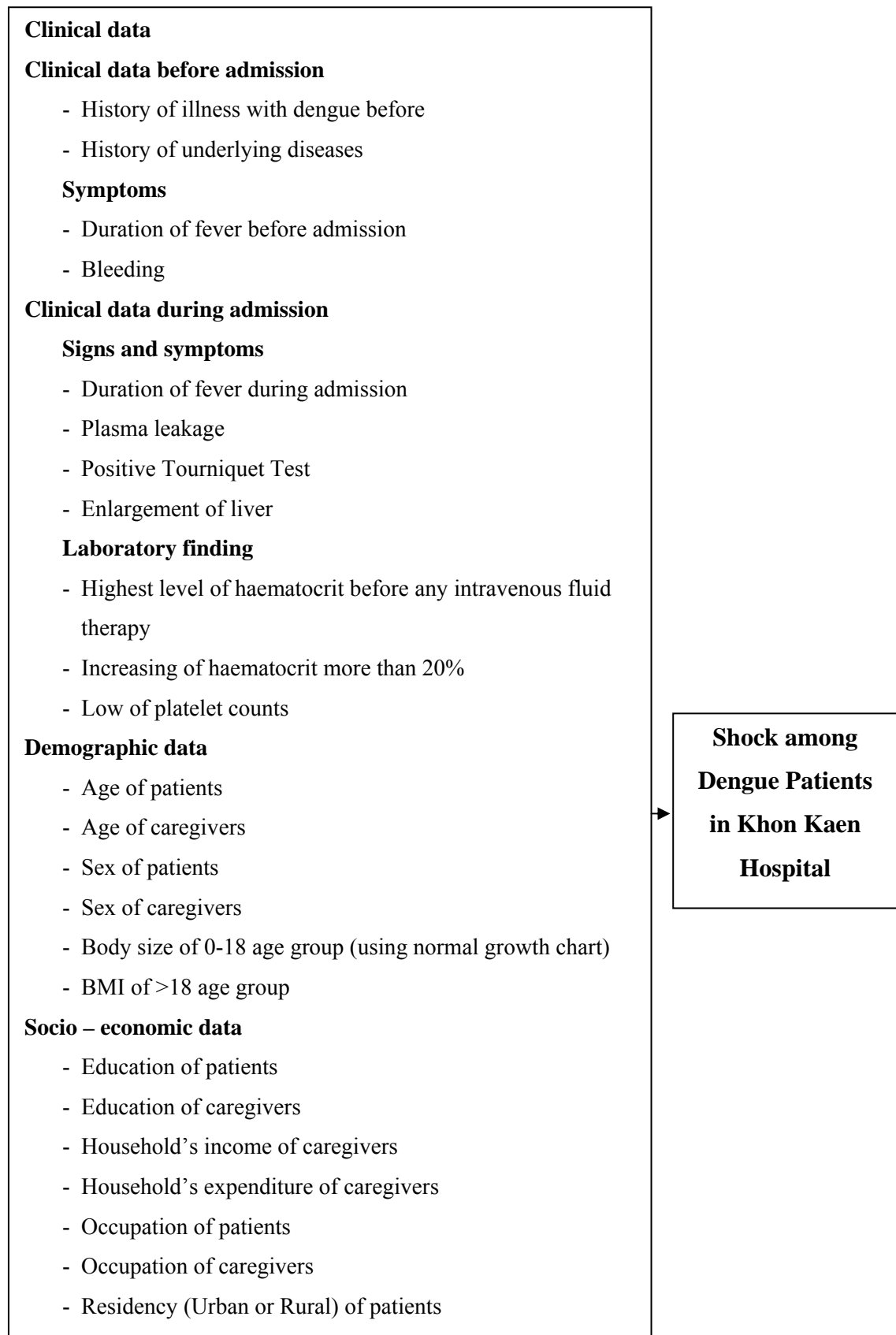
At the present time, DF, DHF and DSS had long been global problems, new knowledge and research for planning to prevent DSS was highly needed. Dengue shock syndrome had impact on physical, mental and economic well being of patients and households. The findings from the study should be useful for health personnel to identify people at risk of developing DSS. It would be useful in identifying generalized factors related to DSS and making generalized manual or guideline for preventing patients from developing DSS. On the other hand, it would expand the knowledge about pathophysiology of DSS.

## **1.7 Assumption of the Study**

The diagnosis of “SHOCK” in DSS in this study was recorded from the medical records under the following criteria:

- 1) Final diagnosis from physicians as DSS
- 2) ICD 10 code of DSS = A913, A914

## 1.8 Conceptual Framework



## 1.9 Operational Definitions

### **Dengue Fever (DF)**

DF was an acute febrile illness of 2-7 day duration (sometimes with two peaks) with two or more of the following manifestations: headache, retro-orbital pain, myalgia/arthralgia, rash, haemorrhagic manifestation (petechiae and positive tourniquet test) and leucopenia (23).

### **Dengue Haemorrhagic Fever (DHF)**

DHF was a probable case of dengue and haemorrhagic tendency evidenced by one or more of the following: positive tourniquet test, petechiae, ecchymosis or purpura, bleeding from mucosa (mostly epistaxis or bleeding from gums), infection sites or other sites, haematemesis or melema. Trombocytopenia (platelets 100,000/cu.mm or less) and evidence of plasma leakage due to increased capillary permeability manifested by one or more of the following: A>20% rise in haematocrit for age and sex, A>20% drop in haematocrit following treatment with fluids as compared to baseline, signs of plasma leakage (pleural effusion, ascites or hypoproteinaemia) (23).

### **Dengue Shock Syndrome (DSS)**

DSS was all above criteria of DHF plus signs of circulatory failure manifested by rapid and weak pulse, narrowing pulse pressure (or equal to <20 mmHg); hypotension for age, cold and clammy skin and restlessness (23).

**Dengue patients** referred to patients with serological test of having DF and DHF admitted in Khon Kaen Hospital during June to November 2007.

**Caregivers** referred to the person(s) that was taking care of the patients before admission to the hospital: father, mother, grandfather, grandmother, aunt, uncle, son, daughter, etc.

**Body size** was used in dengue patients with age  $\leq$  18 years old. It referred to character or size of the body, which indicates nutritional status of the children. Body size was divided into two conditions as follows:

Good nutritional condition meant the state that the body received all useful nutrients in the proper ratio and sufficient quantity, which contribute to good health.

Bad nutritional condition meant the state that the body received insufficient nutrients or exceed nutrients. This condition was as follows:

Malnutrition meant the state that the body received insufficient nutrients, one or more than one nutrient, sometimes it included insufficient energy too.

Over nutrition meant the state that the body received excess nutrients, then they were stored in the body until they caused some disease such as fat disease, hypervitaminosis A and D, etc.

Body size was defined by normal growth chart using weight for age and weight for height scale and categories were divided into three groups as follows:

Normal (Value between Mean  $\pm$  1.5 SD)

Malnutrition or thin (Value less than Mean -1.5 SD)

Fat (Value higher than Mean + 1.5 SD) (24).

**Body Mass Index** was used in age of dengue patients more than 18 years old. It was a number calculated from a person's weight and height. It was a reliable indicator of body fatness for people. BMI did not measure body fat directly, but research had shown that BMI correlated to direct measures of body fat. The calculation was based on the following formulas:  $\text{weight (kg)} / [\text{height (m)}]^2$ . BMI was classified to 5 groups as follows (25):

BMI Classification	
<b>Classification</b>	<b>BMI kg/m<sup>2</sup></b>
Underweight	<18.5
Normal	18.5 – 22.9
At risk Overweight	23 – 24.9
Obesity I	25 – 29.9
Obesity II	$\geq$ 30

**Residency area** meant patient residence which was divided as urban area (living in Muang district) and rural area (living out of Muang district) of Khon Kaen and other province.

**Duration of having fever during admission** meant the duration (days) from the first day that the patient having fever (In the morning  $> 37.3^{\circ}\text{C}$ , in the afternoon  $> 37.8^{\circ}\text{C}$ ) during admission.

**Duration of fever before hospitalization** meant the duration (days) from the first day that the patient got fever until he/she was admitted to hospital.

**History of illness with dengue before** meant the character of Dengue infection in each patient. It meant the dengue patient was infected with at least one serotype of Dengue virus before this recent infection (26). The data were collected from interviewing the patients.

**Symptoms** meant the clinical symptoms found in dengue patients such as fever, headache, anorexia, nausea/vomiting, myalgia, retro-orbital pain, abdominal pain, vascular leakage, gum bleeding, epistaxis, GI bleeding (hematemesis, melena, etc.) (27). The data were collected from interviewing the patients.

**Signs** meant the clinical signs found in dengue patients such as plasma leakage, positive tourniquet test and enlargement of liver, etc. (27).

**Bleeding** meant the symptoms of patient before admission in Khon Kaen hospital such as red spots on the skin, spontaneous bruises, nose bleeding, gum bleeding other bleeding. The data were collected from interviewing the patients.

**Laboratory findings** meant the laboratory findings in dengue patients such as hematocrit (Hct.), WBC and platelet counts (27). The data were retrieved from medical records.

**Plasma leak** referred to evidence of plasma leakage due to increased capillary permeability manifested by one or more of the following (23): The data were collected from interviewing the patients.

- A > 20 % rise in haematocrit for age and sex
- A > 20 % drop in haematocrit following treatment with fluids as compared to baseline
- Signs of plasma leakage (pleural effusion, ascites or hypoproteinaemia)

**Positive Tourniquet Test** was performed by inflating a blood pressure cuff to a point mid-way between the systolic and diastolic pressures for five minutes. A test was considered positive when 10 or more petechiae per 2.5 cm<sup>2</sup> (1 inch) were observed. In DHF, the test usually gave a definite positive result (i.e. > 20 petechiae) (23). The data were retrieved from medical records.

**Enlargement of liver** referred to symptom of having enlargement of liver from palpable at the inferior edge of liver under right costal margin at mid clavicular line (27). The data were retrieved from medical records.

**Highest level of haematocrit before any intravenous fluid therapy** referred to highest level of haematocrit of dengue patients before any intravenous fluid therapy during admitted in Khon Kaen Hospital. The data were retrieved from medical records.

**Increasing of haematocrit** referred to symptom of having of haematocrit increasing was 20% rise in haematocrit for age and sex or 20% drop in haematocrit following the treatment with fluids as compared to baseline (23). The data were retrieved from medical records.

**Low of platelet counts** referred to platelet counts in 100,000/cu.mm or less (2). The data were retrieved from medical records.

## **CHAPTER 2**

### **REVIEW OF THE LITERATURE**

This chapter presents the literature about dengue disease for support this study. The literature was with respect to the following topics; clinical manifestation and diagnosis of DF/DHF/DSS, Severity Grading of Dengue Syndrome, treatment of DF/DHF/DSS and factors associated with DSS.

#### **2.1 Clinical Manifestation and Diagnosis of DF/DHF/DSS**

##### **Dengue Fever**

###### *Clinical Symptoms*

After an average incubation period of 4-6 days (range 3-14 days) there is an abrupt onset of fever, chills, headache, and general malaise. Another common symptom is retroocular pain accentuated by eye movements, photophobia, backache and pain in the muscles and joints/bones of the extremities, anorexia, nausea and vomiting. Arthralgias may be severe, which is why dengue fever is also known as break bone fever. The other common symptoms include anorexia and altered taste sensation, constipation, colicky pain and abdominal tenderness, dragging pains in the inguinal region, sore throat, and general depression. These symptoms vary in severity and usually persist for several days. The high index of suspicion based on period, population & place and absence of convincing evidence of any other febrile illness (3-6).

Towards the end of the febrile period or immediately after defervescence, the generalized rash fades and localized clusters of petechiae may appear over the dorsum of the feet, on the legs, and on the hands and arms, this confluent petechial rash is characterized by scattered, pale, round areas of normal skin. Occasionally the rash is accompanied by itching. The clinical signs are skin bleeding in the form of petechiae and purpura, retro-orbital pain (10).

Convalescence may be short and uneventful, but may also often be prolonged. In adults, it sometimes lasts for several weeks and may be accompanied by pronounced asthenia and depression. Bradycardia is common during convalescence. Haemorrhagic complications, such as epistaxis, gingival bleeding, gastrointestinal bleeding, haematuria and hypermenorrhoea, may accompany epidemics of DF (3).

The clinical features of DF frequently depend on the age of the patient. Infants and young children may have an undifferentiated febrile disease, often with a maculopapular rash. Older children and children and adults may have either a mild febrile syndrome or the classic incapacitating disease with high fever of abrupt onset, sometimes with 2 peaks (saddle – backed). Skin haemorrhages (petechiae) are not common. Leukopenia is usually seen and thrombocytopenia may be observed. Recovery may be associated with prolonged fatigue and depression, especially in adults. Unusually severe bleeding can cause death in such cases. The case-fatality rate of DF, however, is less than 1%. It is important to differentiate cases of DF with unusual bleeding from cases of DHF with increased vascular permeability, the latter being characterized by haemoconcentration. In many endemic areas, DF must also be differentiated from Chikungunya fever, another vector-borne virus disease of similar epidemiology and overlapping distribution in much of Asia and the Pacific (28).

#### *Clinical Laboratory Findings*

The laboratory findings during an acute DF episode of illness are as follows:

Total WBC is usually normal at the onset of fever; then leucopenia develops and lasts throughout the febrile period.

Platelet counts are usually normal, as are other components of the blood clotting mechanism. However, thrombocytopenia is common in some epidemics.

Serum biochemistry and enzymes are usually normal, but liver enzyme levels may be elevated.

**Differential Diagnosis:** The differential diagnosis associated with DF include a wide variety of viral (including Chikungunya), bacterial, rickettsial and parasitic infections that produce a similar syndrome. It is impossible to diagnose mild dengue

infection clinically, particularly when there are only sporadic cases. A definitive diagnosis is confirmed by virus isolation and/or serology (3).

#### *Pathogenesis and Pathophysiology*

The main pathologic findings are endothelial cell swelling in the small vessels of the papillary dermis, diapedesis of neutrophils, extravasation of erythrocytes, perivascular edema, and mononuclear cell infiltrates. There is also a degeneration of endothelial cells and neutrophils. The pathogenesis of this coetaneous eruption is not known (6).

### **Dengue Haemorrhagic Fever and Dengue Shock Syndrome**

#### *Dengue Haemorrhagic Fever (DHF)*

Typical cases of DHF are characterized by high fever, haemorrhagic phenomena, hepatomegaly, and often circulatory failure. Moderate to marked thrombocytopenia with concurrent haemoconcentration are distinctive clinical laboratory findings. The major pathophysiological change that determines the severity of disease in DHF – and differentiates it from DF- is the leakage of plasma, as manifested by an elevated haematocrit (i.e. haemoconcentration), a serous effusion or hypoproteinaemia. Some DHF patients complain of sore throat, and an injected pharynx may be found on examination. Epigastric discomfort, tenderness at the right costal margin, and generalized abdominal pain are common (3).

The temperature is usually high ( $>39^{\circ}\text{C}$ ) and remains so for 2-7 days. Occasionally, temperature may be as high as  $40 - 41^{\circ}\text{C}$ ; febrile convulsions may occur, particularly in infants. The critical stage of the disease course is reached at the end of the febrile phase. After 2-7 days of fever, a rapid fall in temperature is often accompanied by signs of circulatory disturbance of varying severity. The patient may sweat, be restless, have cool extremities and show some changes in pulse rate and blood pressure. In less severe cases, these changes are minimal and transient, reflecting a mild degree of plasma leakage. Many patients recover spontaneously, or after a short period of fluid and electrolytes therapy. In more severe cases, when plasma loss is critical, shock ensues and can progress to profound shock and death if not properly treated (28).

The liver is usually palpable early in the febrile phase, varying from just palpable to 2-4 cm below the right costal margin. Liver size is not correlated with disease severity, but hepatomegaly is more frequent in shock cases. The liver is tender, but jaundice is not usually observed, even in patients with an enlarged, tender liver. In some epidemics, hepatomegaly is not a consistent finding. Splenomegaly is rarely observed in infants under six months, however, the spleen is sometimes prominent on X-ray examination. Chest X-rays show/reveal pleural effusion, mostly on the right side, as a constant finding. The extent of pleural effusion is positively correlated with disease severity (3).

Hemorrhagic manifestations are positive tourniquet test, skin hemorrhages, epistaxis and gum bleeding. The present of thrombocytopenia with concurrent hemoconcentration differentiates grade I and II DHF from classic dengue fever. The patient with DHF can have fever for two to seven days with various non – specific symptoms but can suddenly deteriorate (6).

Convalescence in DHF with or without shock is short and uneventful. Even, in cases with profound shock once the shock is overcome. The surviving patients recover within two to three days. The return of appetite is a good prognostic sign. Common findings in convalescence include sinus bradycardia or arrhythmia and the characteristic dengue confluent petechial rash as described for DF (3).

#### *Dengue Shock Syndrome (DSS)*

The condition of patients who progress to shock suddenly deteriorates after a fever of 2 – 7 days' duration. This deterioration occurs at the time of, or shortly after, the fall in temperature- between the third and the seventh day of the disease (28).

DHF grade IV had evidence of plasma leakage and shown by 20% in haematocrit, hepatomegaly, pleural effusion, ascites, cold perspiration, severe liver involvement and right – upper quarter abdominal tenderness and confusion (7) (8) (9). The other symptom was manifestations of respiratory difficulty, melena, haematemesis, cold clammy skin, narrow pulse, pressure, prolong capillary refill, shock, tachycardia, coma and tourniquet test (10). The hypotension for age, cold clammy skin, restlessness, rapid weak pulse, narrow pulse pressure ( $\leq$  mm of Hg) and profound shock (4).

Patients may pass into a stage of profound shock, with the blood pressure or pulse becoming imperceptible. However, most patients remain conscious almost to the terminal stage. The duration of shock is short: typically the patient dies within 12 – 24 hours, or recovers rapidly following appropriate volume-replacement therapy. Pleural effusion and ascites may be detected by physical examination or radiography. Uncorrected shock can give rise to a complicated course, with the development of metabolic acidosis, severe bleeding from gastrointestinal tract and other organs, and a poor prognosis. Patients with intracranial haemorrhages may convulse and enter a coma. Encephalopathy, reported occasionally, can occur in association with metabolic and electrolyte disturbances or intracranial bleeding.

Convalescence in patients with corrected DSS is short and uneventful. Even in cases of profound shock, once shock is overcome, surviving patients recover within 2-3 days, although pleural effusion and ascites may still be present. Good prognostic signs are adequate urine output and the return of appetite (3).

#### *Pathogenesis and Pathophysiology of DHF and DSS*

The pathogenesis of DHF is not fully understood, but two main pathophysiologic changes occur: Increase vascular permeability resulting in plasma leakage, hypovolaemia and shock. DHF appears unique in that there is selective leakage of plasma into the pleural and peritoneal cavities and the period of leakage is short (24-48 hours). It has been hypothesized that the severity of DHF compared with DF is explained by the enhancement of virus multiplication in macrophages by heterotypic antibodies resulting from a previous dengue infection. There is evidence, however, that viral factor and a cell-mediated immune response are also involved in the pathogenesis of DHF (3).

There are at present two hypothesis of the pathogenesis of DHF. The first one states that the infection virus determines the severity of disease, with virulence varying among different strains (antigenic variation). There is no clear evidence to support this concept since studies done in Asia demonstrated that hemorrhagic disease can occur with strains of any serotypes. The second hypothesis, which is the most widely mediated pathogenesis in which antibody mediated enhancement of the viral infection causes DHF. It is thought that large – scale release of soluble TNFR may be an early and specific marker of the endothelial changes that cause DSS. The mechanism for DSS is not

clearly understood. There appears to be no evidence of injury to the vasculature during infection. The short-lived nature of the plasma leakage in DSS suggests that altered permeability of the blood vessels is most likely due to a soluble mediator (6).

The cut-off point between Dengue Fever and Dengue Hemorrhagic Fever is the evidence of plasma leakage, which will not be present in the former but invariable in the later (4).

#### *Clinical Laboratory Finding of DHF*

The laboratory findings in DHF are as follows:

The WBC may be normal, but leucopenia is common initially, with neutrophils predominating. Towards the end of the febrile phase there is a drop in the total number of white cells as well as in the number of polymorphonuclear cells. A relative lymphocytosis with more than 15% atypical lymphocytes is commonly observed towards the end of the febrile phase (critical stage) and at the early stage of shock.

Thrombocytopenia and haemoconcentration are constant findings in DHF. A drop in platelet count to below  $100,000/\text{mm}^3$  is usually found between the third and eighth days of illness. A rise in haematocrit occurs in all DHF cases, particularly in shock cases. Haemoconcentration with haematocrit increased by 20% or more is considered objective evidence of increased vascular permeability and leakage of plasma. It should be noted that the level of haematocrit may be affected by early volume replacement and by bleeding. A transient mild albuminuria is sometimes observed. Occult blood mild albuminuria is sometimes observed.

In most cases, assays of coagulation and fibrinolytic factors show reductions in fibrinolytic factors show reductions in fibrinogen, prothrombin, factor VIII, factor XII, and antithrombin III. A reduction in antiplasmin (plasmin inhibitor) has been noted in some cases. In severe cases with marked liver dysfunction, reduction is observed in the vitamin K-dependent prothrombin family, such as factor V, VII, IX and X.

Partial thromboplastin time and prothrombin time are prolonged in about one-half and one-third of DHF cases respectively. Thrombin time is also prolonged in severe cases. Serum complement levels are reduced.

Other common findings are hypoproteinemia, hyponatremia, and mildly elevated serum aspartate aminotransferase levels. Metabolic acidosis is frequently found

in cases with prolonged shock. Blood urea nitrogen is elevated in the terminal stage of cases with prolonged shock (3).

## 2.2 Severity Grading of Dengue Syndrome

### *Case Definitions for Clinical Management of Dengue Fever*

Dengue fever is an acute febrile illness of 2-7 days duration sometimes with two peaks having the following manifestations:

1. Sudden onset continuous fever
2. Two or more of the following features:
  - a. Severe headache
  - b. Retro-orbital pain
  - c. Severe myalgia/arthralgia/back pain
  - d. Hemorrhagic manifestations
  - e. Nausea/vomiting/abdominal pain
  - f. Leucopenia
3. High index of suspicion based on Period, Population & Place
4. Absence of convincing evidence of any other febrile illness

### *Severity Grading of Dengue Syndrome*

<b><u>Syndromes</u></b>	<b><u>Grade</u></b>	<b><u>Clinical features</u></b>	<b><u>Laboratory features</u></b>
DF		Features of DF as per case definition	- Leucopenia - $\pm$ Thrombocytopenia - No change in hematocrit
DHF	I	Features/History of features of DF + Positive Tourniquet Test	- Thrombocytopenia $< 100,000/\text{mm}^3$ - Hematocrit rise $\geq 20\%$
DHF	II	Features/History of features of DF	- Thrombocytopenia $< 100,000/\text{mm}^3$ - Hematocrit rise $\geq 20\%$

<u>Syndromes</u>	<u>Grade</u>	<u>Clinical features</u>	<u>Laboratory features</u>
		+ Spontaneous bleeding	
DHF(DSS)	III	Features/History of features of DF + Features of circulatory failure	- Thrombocytopenia < 100,000/mm <sup>3</sup> - Hematocrit rise ≥ 20%
DHF(DSS)	IV	Features/History of features of DF + Profound shock	- Thrombocytopenia < 100,000/mm <sup>3</sup> - Hematocrit rise ≥ 20%

DHF Grade III & IV are also called Dengue Shock Syndrome (DSS) (4).

### 2.3 Treatment of DF/DHF/DSS

#### *Febrile Phase: Therapy*

DF and DHF are not distinguishable in febrile phase and treatment is essentially the same. The modality of treatment is symptomatic and supportive. There are:

Rest, Antipyretic therapy for fever above 39 ° C (Sponging: With tepid water at room temperature, Paracetamol not more than 4 times in 24 hours) according to age.

Do not give Aspirin or any other NSAID. These drugs may cause gastritis and or bleeding. In children, Reye's syndrome may be a serious complication. Do not give antibiotics as these do not help. Oral Rehydration Therapy (ORT) with Oral Rehydration Salt (ORS) or its equivalent is recommended for patients with moderate dehydration caused by vomiting and high temperature. Food should be given according to appetite. But fresh fruit juice should be given frequently. Avoid commercially available fruit juices because these contain preservatives. In case of infant and children if there is febrile convulsion and or history of so appropriate standard measures should be taken.

#### Febrile Phase: Monitoring and Observation

All dengue patients must be carefully observed for complications for at least 2 days after recovery from fever. This is because life – threatening complications often occur during this phase. Patients and households should be informed that severe abdominal pain, passage of black stools, bleeding into the skin or from the nose or gums,

sweating, and cold skin are dangerous signs. If any of these signs are noticed, the patient should be taken into the hospital. The patient who does not have any evidence of complications and who has been afebrile for 2 – 3 days does not need further observation.

#### Afebrile Phase: Dengue Fever

Constitutional symptoms in patients with DF after the fall of fever are similar during the febrile phase. Most patients will recover without complications. The following manifestations may be present: Improvement in general condition, platelet, hematocrit normal and appetite rapidly regained. Management is more or less the same, ie continue bed rest, check platelet and hematocrit; fruit juices, oral fluid and electrolytes therapy.

#### Convalescent Phase: Dengue Fever

The duration of convalescence phase is 7 – 10 days after the afebrile phase. During this phase further improvement in general condition and return of appetite occur. Bradycardia and confluent petechial rash with white center and or itching may persist. Weakness may remain up to another week or two. No special advice is necessary. No restriction is also needed. Normal diet and effort for adjusting to normal life style and work are what is necessary.

#### *Critical Phase: DHF*

During the afebrile phase usually the features of DHF evolve, which are various bleeding manifestations, signs of circulatory failure and, progressive thrombocytopenia and plasma leakage as manifested by rise in hematocrit. Depending on the grading of severity the management should be instituted immediately to avoid fatality. Therefore this period is very crucial. Moreover the only difference between DF and DHF Grade I is the presence of thrombocytopenia and rise in hematocrit > 20%. Patients with DHF Grade I do not usually require intravenous fluid therapy and ORT is sufficient. Intravenous fluid therapy may need to be administered only when the patient is vomiting persistently or severely, or refuses to accept oral fluids. Patients with DHF Grade I who live far away from the hospital or those who are not likely to be able to follow the medical advice should be kept in the hospital for observation.

During the afebrile phase of DHF Grade II, the complications usually seen, in addition to those observed during DHF Grade I phase, are abdominal pain, blacky tarry stools, epistaxis, bleeding from the gum, and continued bleeding from the injection sites.

Immediately after hospitalization, hematocrit and platelet count must be carried out to assess the condition of the patient. A reduction in platelet count to  $\leq 100,000/\text{mm}^3$  or less than 1 – 2 platelets/oil field (average of 10 oil field counts) usually precedes a rise in hematocrit. A rise in hematocrit of 20 % or more (eg increase from 35% to 45%) reflects a significant plasma loss and indicates the need for intravenous fluid therapy. Early volume replacement of lost plasma with Grystalloid solution (eg isotonic saline solution) can reduce the severity of the disease and prevent shock. Intravenous fluid therapy before leakage is not recommended. But in DHF Grade II depending on the condition IV therapy may be given for 12 – 24 hours. Medical personnel should monitor patients on hourly basis. Based on periodic hematocrit/platelet count determinations and vital signs, the treatment should be reviewed and revised.

*Critical Phase: DHF III and IV Therapy*

Common signs of complication observed during the a febrile phase of DHF Grade III include circulatory failure manifested by rapid and weak pulse narrowing of the pulse pressure and hypotension, characterized by high diastolic pressure relative to systolic pressure (eg 90/80) and the presence of cold clammy skin and restlessness. Immediately after hospitalization the hematocrit, platelet count and vital signs should be examined to assess condition of the patient, and intravenous fluid therapy should be started. The patient requires regular and sustained mentoring. If the patient has already received about 1,000 ml of intravenous fluids and the vital signs are still not stable, hematocrit should be repeated and: (a) if the hematocrit is increasing intravenous fluid should be changed to colloidal solution preferably Dextran, or (b) if hematocrit is decreasing, fresh whole blood transfusion 10 ml/kg/dose should be given.

During the afebrile phase of DHF Grad IV vital signs are unstable. The patients, in the early stage of shock, had acute abdominal pain, restlessness, cold and clammy skin, rapid and weak pulse. The patient should be administered intravenous fluid therapy immediately. In case of continued or profound shock when pulse and blood pressure are undetectable, the patient should be given colloidal fluid following the initial fluid bolus.

However, in the case of persistent shock when, after initial fluid replacement and resuscitation with plasma expanders, the hematocrit continues to decline, internal

bleeding should be suspected. It may be difficult to recognize and estimate the degree of internal blood loss in the presence of hemoconcentration. It is thus recommended to give fresh whole blood in small volumes of 10 ml/kg body weight at one time. Blood grouping and matching should be done for all patients in shock as a routine precaution. Oxygen should be given to all patients in shock (4).

## 2.4 Factors Associated with DSS

### 2.4.1 Sex of Patients.

#### *Female was Decreasing Risk to DSS more than Male*

A case control study at Children's Hospital Bangkok in 1992, determining the risk factors of Dengue Shock Syndrome found that females were 55.4% of DSS patients and 35.9% in DHF patients, there was also statistically significant association with OR = 2.04, 95% CI = 1.08 – 3.85,  $P = 0.0176$  (29).

Study on sites in northern Thailand, found females had more than half the risk of seropositivity compared with males (adjusted OR = 0.45, 95% CI = 0.21 – 0.94) (30).

An epidemic of dengue haemorrhagic fever (DHF) occurred in Delhi in 1996. A total of 240 children between the age of 4 months to 13 years of either sex, admitted in one hospital, were evaluated. The girls were more severely affected as compared to boys ( $p < 0.01$ ) (31).

Kabra et al. found that the girls were more severely affected as compared to boys ( $p < 0.01$ ) (31).

The retrospective epidemiological study in Malaysia found that higher case fatality rate in females (32).

An observational, cross-sectional study was conducted on DSS cases hospitalized at the Paediatric Intensive Care Unit, Jakarta, during January – June 1998. There were 188 DSS cases included in this study of which 46.1 % were males and 53.9% females (33).

*Male was Decreasing Risk to DSS more than Female*

Muldives record in the 1999, out of the 52 DF and 26 DHF cases reported from Indira Gandhi Memorial Hospital, it was surprising that for both the DF and DHF infections males suffered 2.7 times and 2.3 times more than females respectively and there is no significant difference in the proportion of infected males suffering from DF and DHF infections ( $X^2 = 0.13$ ,  $P = 0.72$ ) (34).

Epidemic found a male to female ratio of 1:0.25 cases for DSS. However, of the three deaths in this sample, two were females (35).

Studied in serotype-specific dengue virus circulation and dengue disease in Bangkok, Thailand from 1973 to 1999. There were proportionately more males (52%) than females (48%) ( $P < 0.001$  by binomial test) (36).

Study on a total of 112 non-paediatric patients at Venezuela during June 1998 – June 2001 found that male/female ratio was 64/48 (37).

*Male and Female were not Significant*

Epidemic in India and Singapore found nearly twice the number of male patients compared to females. Lucknow and Singapore both report male to female ratios of 1.9 : 1 (38) and Delhi 1 : 0.57 (35).

As part of a multi-center, prospective study of dengue pathophysiology between 1994-1997, Thailand, the male/female ratios for dengue and other febrile illness patients were 1 : 1.12 and 1 : 1.45, respectively (39).

Witayathawornwong and Pancharoen et al. studied Dengue in infant patients at Pechaboon Hospital and King Chulalongkorn Memorial Hospital. They found the sex ratio of male and female were 1 : 1.6 and 1 : 2.1 respectively (40).

No gender difference was observed in the DF, DHF or DSS patients in a retrospective review of patients who were admitted to the Children's Hospital between 1995-1999 (8).

A study in Ho Chi Minh City, Vietnam during August 1997 to December 2002 found sex in infants with DHF or DSS in the study is not different from that of healthy control subjects (Odds ratio (OR) = 1.20, 95% confidence interval (CI) = 0.88 - 1.65,  $P = 0.2$ ) (41).

During the months of September 1993 through February 1994, an outbreak of hemorrhagic fever in Irian jaya, Indonesia found that the pediatric patient population consisted of 36 individuals ages 1-12 years of age with a similar male to female ratio (7).

#### **2.4.2 Age of Patients**

*Age Distribution of Dengue Patients was Highest in 5 – 9 Years.*

Okanurak et al. studied the treatment seeking behavior of DHF patients in Thailand. From 184 cases from 3 hospitals; Children's Hospital, Bangkok; Suphan Buri Provincial Hospital, and Don Chedi Community Hospital in Don Chidi district, Suphan Buri province. They found that the most patients were in the age of 6 months to 14 years old. There were only 3 cases older than 14 years old, but the biggest group of these cases is 5-9 years old (42). Several studies have shown that a majority of the DHF cases occurred in children in the age-groups 5-9 years (37.4%) and 10-14 years (28.7%) (42).

A case control study at Children's Hospital Bangkok in 1992, determined risk factors of Dengue Shock Syndrome found dengue patients in 5-9 years age-group had developing to Dengue Shock Syndrome more than 0 – 4 years with Odds Ratio (OR) = 2.75, 95% CI = 1.08 – 3.85 and  $P = 0.0050$ ) (29).

The overall age-specific incidence rate of DHF in a retrospective epidemiological study 1973-1987 in Malaysia was highest in two age group, viz. 5-9 years and 10-19 years of age with a mean morbidity rate of 4.9 cases per 100,000 (32).

Study on treatment of dengue haemorrhagic fever at Children's hospital, Ho Chi Minh City, Viet Nam found the age-wise distribution of DHF patients in 1996. A majority of DHF cases occurred in children in the age – group 5-9 years (37.4%) and 10-14 years (28.7%) (43).

An observational, cross-sectional study was conducted on DSS cases hospitalized at the Paediatric Intensive Care Unit, Jakarta, during January – June 1998. The age group distribution was: 10 cases were below 1 year of age, 1-4 years old accounted for 29% while those above 10 years accounted for 15.40%. The highest proportion of the cases (40%) belonged to the 5 – 9 years of age group (33).

From study in Indonesia about epidemic dengue transmission, children aged 10-19 years accounted for the largest proportion of all patients with DF (33% of 660

cases) and DHF (35% of 1,772 cases), while children aged 5-9 years accounted for the largest portion of DSS (40% of 253) (44).

As part of a multi-center, prospective study of dengue pathophysiology between 1994-1997, the mean age for DF, DHF grad I, DHF grade II, DHF grade III and other febrile illness patients were 8.01 ( $\pm 2.93$ ), 8.25 ( $\pm 3.58$ ), 8.9 ( $\pm 2.86$ ), 7.48 ( $\pm 2.4$ ) and 6.59 ( $\pm 3.15$ ) years (39).

Dengue virus circulation and association with epidemics and severe dengue disease were studied in hospitalized children with suspected dengue at the Queen Sirikit National Institute of Child Health in Bangkok, Thailand. The mean age of patients with dengue was 7.6 years (range 1.1 to 17 years, SD 3.4 years). The overall modal age was 6 years, which also increased over time from 5 years during 1973-79 to 8 years during 1990-99 ( $\beta = 0.50$ ,  $P = 0.008$  by linear regression) (36).

A retrospective review was done of 5,332 patients at the Children's Hospital, Bangkok found that the mean age for DF case was observed as 7.9 years, DHF 8 years and DSS 8.1 years. The mean age for DHF and DSS was the same ( $P > 0.46$ ). There was a significant increase in the mean age of dengue patients from 7.6 years in 1995-1996 to 8.1 – 8.2 years in 1997-1999 (8).

Muldives record in the 1999, out of the 52 DF and 26 DHF cases reported from Indira Gandhi Memorial Hospital, the majority of the cases ( $34/52 = 65.4\%$ ) and ( $23/26 = 88.5\%$ ) occurred, respectively, in children less than 10 years of age (34).

*Many Reserches found that the Highest of Age Dengue Patients was the Children Age under 15 Years Old.*

Kantacchuvessiri's study found about 65% of total cases of Thailand were the children whose ages were 5-14 years old, since the increasing of breeding place and there are some Dengue out breaks in school (45).

Kalyanoroj et al. studied Dengue patients at Children's Hospital, Bangkok: 1995-1999 Review. The means of ages of DHF and DSS cases were similar (DHF 8 year old, DSS 8.1 years old), but DSS would increase in the group of 10-14 years old ( $p > 0.46$ ) (46).

A retrospective study of 347 patients with serologically confirmed dengue infection admitted to Chonburi Hospital during an epidemic in 2001. The median age of the patients was 10 years; range: 4 months to 66 years. The most frequent age groups were 10-14 years (37%), 4-9 years (36%) and 15-24 years (15%). Severe infection was significantly more common in adult patients (82% vs. 59% in children,  $P < 0.001$ ) (9).

From current status of dengue /dengue haemorrhagic fever in WHO South – East Asia, about the age distribution shown in Sri Lanka that 70 % of the cases were related to those less than 15 years of age with the peak being seven years. Thailand affected the younger age-groups of the less than 15 years with the highest proportion of case occurring in the age-group 5-9 years, follow by the age-group 10-14 years. In Myanmar, the DF and particularly DHF/DSS were increasingly becoming serious public health problems, especially among the 5-10 and 11-15 years old and the highest age-group was 5-8 years old (20).

Study on Predictive Indicators for Forecasting Epidemic of Dengue/ Dengue Haemorrhagic Fever through Epidemiological, Virological and Entomological Surveillance found DF/DHF cases in 1998 and 1999 occurred mostly in children under 15 years of age. Shock accounted for 15.3% and 13.5% of all cases of DF/DHF in 1998 and 1999 respectively, while 2.5% and 2.1% of the shock cases died (47).

Effect of increasing age on the trend of dengue and dengue hemorrhagic fever in Singapore found the DHF/DF ratio increased exponentially with the increase in the proportion of cases less than 15 years of age ( $R^2 = 0.81$ ) (48).

An epidemic of dengue haemorrhagic fever occurred in Delhi in 1996. A total of 240 children between the age of 4 months to 13 years of either sex. The mean age was  $6.7 \pm 3.12$  years. As many as 22 (9%) were infants. The peaked at 8 years (49).

Six hundred and fifty DHF/DSS cases were hospitalized during 1994 – 1995, DSS was diagnosed in 81 patients, most DSS cases belonged to under 14 years of age group, 76 (94%) of 81 DSS cases. DSS cases were significantly younger than DHF cases ( $P = 0.001$ ) (50).

The data from The Children's Hospital in Indonesia indicated 188 cases that had shock syndrome (DSS) also, 50.3% of these were the group of more than 10 years old, 29% were 1-4 years old. In addition, it found that the group of under 1 year old had the highest death rates when the disease came to the shock stage (46).

*Many Researches Suggest That in Older Age Group was Higer Proportion in Dengue Patients.*

A prospective study of dengue fever and dengue hemorrhagic fever was conducted in a cohort of adult volunteers from two textile factories located in West Java, Indonesia. This study had a mean age of the DEN cases was 37 years old (range = 18-64 years) in Grandtex and 33 years old (range = 18-66 years) in Naintex (5).

Study investigation the clinical manifestations and risk factors for dengue fever and dengue hemorrhagic fever and disease severity during the 2002 outbreak in the Kaohsiung area. The mean age of patients with DHF/DSS was  $53.6 \pm 16.3$  years, and the highest incidence occurred in those age 60-69 years (27.2%). Significant risk factors for DHF/DSS were age >65 years (51).

Study on a total of 112 non-paediatric patients at Venezuela during June 1998 – June 2001 found that the age range was 15- 92 years; median 36 years (37).

Between December 1997 and March 1999 in far North Queensland, Australia. The mean age of 100 dengue patients was 42.5 (range 1 – 76) years. Patients with secondary infections were older ( $P < 0.01$ ) (52).

Study on sites in northern Thailand, found persons  $\geq 30$  years old had more than five times a highest risk of being seropositive compared with persons  $< 30$  years old. Comparable with Ban Pa Nai, the prevalence of antibodies in Ban Pang was significantly related to age ( $P = 0.002$ ) (30).

A prospective cohort study was analyzed both an ecological study and in terms of risk to individuals found the age distribution of the studied cases showed that lowers in the age groups : 29.0% among 0 – 4 years old and reaching a maximum of 76.4% in the 30 – 39 years old. The incidence of infection was lower in the group aged 0 – 4 (46.2%), but showed a sharp increase in the next age group (5 – 9 years old) (78.3%) and maintained levels between 62.7% and 82.8% in the older age groups (53).

### **2.4.3 Secondary Infection of DHF**

In descending order of magnitude, risk factors for dengue shock syndrome in Rayong were secondary infection with dengue 2 which followed primary infections with dengue 1, dengue 3, or dengue 4. The association of initial dengue 1 infection with

subsequent secondary infection-associated dengue shock syndrome is significant. ( $p$ -value  $< 0.02$ ) (54).

Thein et al. studied during five years among 385 children from Thamwe and Alphone were admitted in Yongon Children's Hospital. They found that 29 patients were classified as primary dengue infection, 166 as secondary dengue infection, and the remaining 114 as not having had recent dengue infection. The ratio of primary to secondary dengue infection in DHF 1 and 2 was 1 : 9.4 and DSS patients was 1 : 46. (55). Messer WB et al. studied epidemiology of dengue in Sri Lanka before and after the emergence of epidemic DHF. The result was shown that secondary infections were associated with an increased risk of development severe disease (OR = 4.25, 95 % CI 0.75 – 23.9) (56).

Kalayanarooj et. al. A retrospective review was done of 5,332 patients who admitted to Children's Hospital (Inpatients Department-IPD) with the diagnosis of DF/DHF between 1995-1999. The result showed DF patients, 38.5% of primary infection and 61.6% of secondary infection while in DHF/DSS patient, 19.1% of primary infection and 80.9% of secondary infection (8).

Vijpayee et al. studied about Dengue virus infection during post-epidemic period in Delhi, India, a study was carried out using virological and serological test for confirmation of suspected cases of dengue virus infection in fever cases presenting to the All India Institute of Medical Science. Serum samples of suspected DF/DHF cases were processed from January to December 1997. The result shown that majority of the cases were secondary dengue fever (57).

Vaughn DW et al. studied about dengue in the early febrile phase: viremia and antibody responses, there was thirty-two percent of these children had dengue infection (60 volunteers). The percentage of children with a secondary dengue infection was 93%, with only 4 (7%) having a primary infection (58).

Viremia titers in serial plasma samples from 168 children with acute dengue virus infection who were enrolled in a prospective study at 2 hospitals in Thailand found that eighty-one percent of patient experienced a secondary dengue infection that associated with more severe disease (59).

Nisalak and others studied in Bangkok, Thailand found that DHF was more likely to result from a secondary than a primary infection (odds ratio, 5.0; 95%

confidence interval 4.5-5.6). Secondary dengue DHF was associated with more severe DHF: grade I (15% of all secondary DHF), grade II (31%), grade III (47%), and grade IV (7%) ( $P < 0.0001$  by  $X^2$  for linear trend) (36).

Studied seroepidemiology of dengue in Indonesian found that six hospitalized children with confirmed DEN virus infections met the case definition of DHF. Five of the six patients hospitalized with confirmed DHF/DSS experienced secondary dengue infections (36).

In studied clinical characteristics of dengue and dengue hemorrhagic fever in Taiwan found that history of dengue infection association with DHF/DSS (51).

Ole Wichmann, Suchart Hongsiriwon et al. studied about risk factors and clinical features associated with severe dengue infection in adult and children, a study found that a secondary dengue infection was associated significantly with the development of DHF in children, OR(95%CI) = 3.63 (1.94-6.82),  $P < 0.001$ , but not in adult, OR(95%CI) = 0.6 (0.02-6.04),  $P = 1.0$ ) (9).

A retrospective review between 1995-1999 at the Children's Hospital, Bangkok found that the secondary infection (77.3%) had percent more than primary infection (22.7%) (8).

Study on secondary dengue virus type 4 infections in Vietnam had a prevalence of primary and secondary acute dengue infection was 4% and 78.4% (60).

As part of a multi-center, prospective study of dengue pathophysiology between 1994-1997, Thailand, found primary and secondary dengue infection were found in 30.64% and 69.36% of DF patients while 9.29% and 90.71% of the primary and secondary dengue infection were found in DHF patients (39).

A case control study at Children's Hospital Bangkok in 1992, determined risk factors of Dengue Shock Syndrome found the secondary infection was also associated with DSS with OR = 4.81, 95% CI = 1.68 – 14.48 and  $P = 0.008$  (29).

From a case control study in Children in BMA Medical College and Vajira Hospital found that the secondary dengue infection was risk to DSS (adjusted OR(95% CI : 21.8 (5.3 – 90.8) (61).

#### **2.4.4 BMI of Patients**

Halstead stated that there was strong association between good nutritional status in children and DSS (62).

Nearly universal anecdotal clinical observations showed that DHF/DSS was rarely seen in children with protein energy malnutrition (PEM) (63).

Thisyakorn et al. studied Nutritional status of children with Dengue hemorrhagic fever Nutritional status was assessed for 100 patients with serologically confirmed dengue hemorrhagic fever (DHF), 125 patients with other infectious disease who were admitted to Children's Hospital (Bangkok), and 184 healthy children. The assessment was done by using with use of the following parameters: weight for age. The prevalence of 13% malnutrition found among patients with DHF is significantly lower than the prevalence of malnutrition found among patients with other infectious diseases and among healthy children. The study confirmed the observation generally middle that most patients with DHF are not undernourished (64).

From study in Ho Chi Minh City, Veitman during August 1997 to December 2002 found infants with DHF had a higher percentage of malnutrition (wasting) as assessed by WH (14.2% versus 1.1 %;  $P < 0.001$ ). With smaller numbers, no statistically significant differences were observed in the distribution of various parameters of undernutrition in the DSS and nonshock DHF group (41).

A hospital based case-control study was conducted from October 2002 to November 2003 among children aged 0-14 years at Queen Sirikit National institute of Child Health, Bangkok found the patients who had obesity were at increased risk for more severe DHF (OR = 2.77, 95% CI 1.19 – 6.45) compared to those at normal weight (26).

Kebra et al. studied Dengue hemorrhagic fever (DHF) occurred in Delhi in 1996. They found that a total of 240 children between the age of 4 months to 13 years of either sex, admitted in one hospital, were evaluated. Two hundred and sixteen (90%) children were from Delhi. A clinical diagnosis of dengue fever (DF) was made in 25(10%), dengue fever with unusual bleeding (DFB) in 22(9%), DHF in 80(33%) and dengue shock syndrome (DSS) in 113 (47%) of the children strictly according to the WHO classification. No association between severity of malnutrition and severity of illness was observed (31).

An epidemic of dengue haemorrhagic fever occurred in Delhi in 1996 found no association between severity of malnutrition and severity of illness was observed (49).

#### **2.4.5 Socio Demographics of Caregivers**

A cross-sectional study was carried out between July 1998 and June 1999 to identify dengue virus-infected patients under age 15 admitted to seven government hospitals in Ang Thong Province a central region of Thailand, and to assess to knowledge, attitude, and practice (KAP) of their caregivers. A total of 131 caregivers of enrolled children were interviewed in the context of KAP in DHF. The majority of them were mothers with primary school education level. Half of the caregivers were workers (65).

Okanurak et al. said that the information was collected by interviewing the patients' caregivers while they were attending the patients in the hospitals, using a series of closed-and open-ended questions. The socio-demographic characteristics of the patient's caregiver that influenced the decision making to take treatment alternatives included the level of education, occupation, residential area and lay symptom assessment. In addition, economic factors: the capability to reimburse the cost of treatment, the family income and the financial sources, were also important for caregivers to take into consideration when making treatment choices (42).

Study in Surabaya, Indonesia, found a significant correlation was found between the household income and the presence of DHF cases with the housewives' knowledge about controlling DHF: every increase of Ro. 100,000 in the household income resulted in better knowledge (as much as 1.34 times), and housewives with the presence of cases had 0.28 times less knowledge than housewives without cases (66).

Shekhar KC and Huat OL found that the mean overall incidence of dengue death in the urban area was 0.5 compared to 0.1 per 100,000 for rural areas (32).

In Khulna Medical Collect Hospital, Bangladesh found the proportion of children with dengue from urban area (57.4%) more than rural area. Regarding school status of affected children, it was found that primary school children were the commonest victims. Majority of patients (59.2%) belonged to average income family (67).

Study on sites in northern Thailand, found in rural sites, older persons had a higher risk of seropositivity and persons living in house surrounded by natural and agricultural land covers had a lower risk of seropositivity and the periurban site, only knowledge of dengue was related with seropositivity. Person ignorant about dengue had a risk twice as high of being seropositive compared with persons with knowledge of dengue (OR = 2.05, 95% CI = 0.99 – 4.28) (30).

“Factors associated with resurgence of Dengue Epidemic are unprecedented growth of population, unplanned and uncontrolled urbanization, inadequate waste management and water supply and increased distribution, densities of vector mosquitoes, lack of effective mosquito control measures and increased movement and spread of dengue virus.” (68).

A case-control study in Fevela in Fortaleza (north-east Brazil) during an outbreak of dengue fever found none of the socio-economic variables (illiteracy, family income, number of persons living in the house, persons per bedroom, lack of piped water, lack of sanitation) was a predictor for the occurrence of dengue fever (OR = 0.6 – 1.55;  $P = 0.4 – 0.8$ ) (69).

#### **2.4.6 Duration of Fever before Hospitalization**

Study on a total of 112 non-paediatric patients at Venezuela during June 1998 – June 2001 found that the length of illness prior to admission was longer (mean 4.35 days vs. 3.26 days;  $P < 0.05$ ) (37).

Between December 1997 and March 1999 in far North Queensland, Australia found the mean duration symptoms prior to admission was 5 (range 1 – 35) days.(52)

Six hundred and fifty DHF/DSS cases were hospitalized during 1994 – 1995, the mean number of fever days before hospitalization was 3.7 days for DHF cases and 4.2 days for DSS cases ( $P = 0.005$ ). Significantly more DSS cases had more than 4 days of fever before admission compared to DHF cases ( $P = 0.02$ ) (50).

Study on DHF in infants age 3-12 months who were admitted to the Department of pediatrics, Chon Buri Regional Hospital, Thailand, during January 1995 to December 1998. They found 20 infants from 983 patients who were under 15 years old. From these 20 infants patients, there were 15 persons who got DHF only, and had got fever for 2-9 days (mean = 4.5 days) before coming to the hospital (70).

#### **2.4.7 Duration of Fever**

From on guideline for diagnosis and treatment in dengue hemorrhagic fever, public health ministry, Thailand found the duration of fever is related to Shock,

some case happen on 3<sup>rd</sup> of symptom (had fever 2 days) or 8<sup>th</sup> of symptom (had fever 7 days) (2).

The clinical features are shown all cases of DF, DHF and DSS had fever of a mean duration of 4.4+1.8 days, 5.0+2.2 days and 4.1+2.7 days respectively. The total days required to become a febrile was 8.0+2.5 days in DF, 9.5+4.5 days in DHF and 6.5+4.9 days in DSS (10).

A retrospective review was done of 5,332 patients who admitted to the Children's Hospital (Inpatients Department-IPD) with the diagnosis among dengue fever (DF)/dengue hemorrhagic fever (DHF) between 1995-1999. Duration of fever in DHF is 5.0 days and DSS is 4.8 days (8)

On study in Chonburi during 2001, Thailand found the mean (SD) duration of fever was 5.4 days (1.4). Fever clearance time was not significantly different between adults and children groups (mean  $\pm$  1.8 days vs.  $5.3 \pm 1.4$  days, respectively,  $P = 0.09$ ) or between the disease severity group ( $P = 0.30$ ) (9).

As part of a multi-center, prospective study of dengue pathophysiology between 1994-1997, Thailand, found the mean duration of fever for DF, DHF grade I, DHF grade II, DHF grade III was 4.08 day ( $\pm 1.19$ ), 4.51 days ( $\pm 0.90$ ), 4.38 days ( $\pm 0.99$ ), 5.27 days ( $\pm 1.72$ ). Among DHF patients 2.16% had fever for 2 days, 10.07% had fever for 3 days, 41.01% had fever for 4 days, 30.94% had fever for 5 days, 11.51% had fever for 6 days and 2.16% had fever for 7 days (39).

Study on treatment of dengue haemorrhagic fever at Children's hospital, Ho Chi Minh City, Viet Nam found fever was a major manifestation of DHF and persist for 2-7 days in almost all cases; a few exceptional cases with fever lasted for more than seven days (43).

Study on headache features in patients with dengue virus infection found that the mean duration of febrile disease was  $6 \pm 2.6$  days (71).

#### **2. 4.8 Underlying Diseases**

Study on dengue patients at the Children's Hospital, Bangkok: 1995-1999 reviews found association conditions 2.7% of all dengue patients, there were thalassemia and G-6-PD deficiency occurrence range from 1.8% in 1996 to 3.5% in 1997 (8).

Min-Sheng Lee et al. found that the proportion of DHF/DSS cases associated with chronic disease such as diabetes mellitus, hypertension or renal insufficiency (uremia) was significantly ( $P < 0.005$ ) higher than for DF cases (16.8% vs. 7.6%, 28.9% vs. 16.3%, and 6.6 % vs. 1.0 %, respectively). Multiple logistic regression analysis revealed a significant association between DHF/DSS diabetes mellitus, hypertension and renal insufficiency (51).

#### **2.4.9 Plasma Leakage**

There are four serotypes of dengue virus produce similar manifestations, which may be asymptomatic, undifferentiated fever, dengue fever (DF), dengue hemorrhagic fever (DHF) with plasma leakage, that may lead to hypovolumic shock, dengue shock syndrome (DSS) (28).

From Guideline for diagnosis and treatment dengue haemorrhagic fever in Thailand and Comprehensive Guidelines for Prevention and Control of Dengue/DHF found that Dengue haemorrhagic fever has a clear pattern clinical such as high fever pulse manifestation, liver enlargement and had shock in severe case. Febrile phase has a symptom like DF but has a specific symptom is lower platelets and plasma leakage, if much of plasma leakage lead to shock (2) (3).

Study on a total of 112 non – pediatric patients at Venezuela during June 1998 – June 2001 found that vascular leakage was also associated with illness severity on a admission in the multivariate regression analysis (OR = 14.3;  $P < 0.005$ ) (37).

#### **2.4.10 Positive Tourniquet test**

A case control study at Children's Hospital Bangkok in 1992, determined risk factors of Dengue Shock Syndrome found positive tourniquet test (OR = 8.56, 95% CI = 1.06 – 188.63 and  $P = 0.0076$ ) (29).

As part of a multi-center, prospective study of dengue pathophysiology between 1994 – 1997, Thailand, found the percentage of TT positive in DF, DHF grade I, DHF grade II, DHF grade III was 87.50%, 90.48%, 94.87%, respectively (39).

The study was conducted on seropositive cases of dengue less than 12 years of age admitted in Chennai, India. The factors related to shock was positive tourniquet test ( $P = 0.0004$ ) (OR = 6.5, 95% CI = 1.4 to 31.9) (72).

#### **2.4.11 Enlargement of Liver**

A case control study at Children's Hospital Bangkok in 1992, determined risk factors of Dengue Shock Syndrome found an enlargement of liver (OR = 5.49, 95% CI = 1.08 – 37.44 and  $P = 0.0169$ ) (29).

Study on treatment of dengue haemorrhagic fever at Children's hospital, Ho Chi Minh City, Viet Nam found hepatomegaly was another major clinical manifestation in DHF. It was observed in 86% of the patients of grad I and II and 98% of DSS cases (43).

The liver is usually palpable early in the febrile phase and varies in size from just palpable to 2-4 cm below the costal margin. Although liver size is not correlated with disease severity, an enlarged liver is observed more frequently in shock than in non-shock cases (3).

#### **2.4.12 Increasing of Hematocrit**

Study on dengue patients at the Children's Hospital, Bangkok found that abdominal pain (1995-99) was the most common complaint in dengue patients (38%) 30.1% for DF, 35.4% for DHF and 49.9% for DSS. In DSS cases evidence of plasma leakage as shown by 20% rise in haematocrit was 63.8% , pleural effusion was found in 96.1% of DSS cases, who had chest X-ray done (8).

A retrospective study in Chonburi Hospital, Thailand found that during hospitalization, there were significant rises of haematocrit levels in both the DF and DHF group ( $P < 0.001$ ), and patients with shock (DSS) had significantly higher peaks of haematocrit level than the other non-shock group ( $P = 0.038$ ) (9).

A case control study at Children's Hospital Bangkok in 1992, determined risk factors of Dengue Shock Syndrome found increase of hematocrit more than 20% (OR = 9.55, 95% CI = 4.63 – 19.88 and  $P = 0.0009$ ) (29).

Study on Hospital of Dr. Mohammad Hoesin, Palembang, South Sumatera, Indonesia about risk factors of dengue shock syndrome in Children Division found a variable including hematocrit value were both statistical significant association with dengue hemorrhagic fever with shock syndrome with Odds ratio 5.96 ( $P = 0.0001$ ) (73).

#### **2.4.13 Decreasing of Platelet Counts**

The median (range) platelet count of all patients on admission was 85,000 (7,000-372,000)/ $\mu\text{l}$ , and with DHF had a significantly lower median platelet count compared with those with DF (69,000/ $\mu\text{l}$  vs. 113,000/ $\mu\text{l}$ ,  $P = 0.001$ ). During hospitalization, platelet counts decreased significantly in all groups of disease severity ( $P \leq 0.001$ ) (9).

A case control study at Children's Hospital Bangkok in 1992, determined risk factors of Dengue Shock Syndrome found the laboratory findings was also found thrombocytopenia less than 100,000/ $\text{mm}^3$  (OR = 8.56, 95%CI = 3.74-20.88 and  $P < 0.001$ ) (29).

The study was conducted on seropositive cases of dengue less than 12 years of age admitted in Chennai, India. The factors related to shock was low platelet count less than 50,000/cm.mm ( $P=0.01$ )(OR = 6.5, 95%CI = 1.4 to 31.9) (72).

Study on Hospital of Dr. Mohammad Hoesin, Palembang, South Sumatera, Indonesia about risk factors of dengue shock syndrome in Children Division found variable including platelet (thrombocyte) was statistical significant association with dengue hemorrhagic fever with shock syndrome with Odds ration 5.53 ( $P = 0.0001$ ) (73).

#### **2.4.14 Bleeding**

From a case control study in Children in BMA Medical College and Vajira Hospital found that bleeding was risk factor of DSS (adjusted OR (95%)CI: 5.1(1.5-17.1) (61).

## **CHAPTER 3**

### **MATERIALS AND METHODS**

The aim of this study was to analyze the association between factors related to dengue shock syndrome (DSS) among dengue fever (DF) and dengue hemorrhagic (DHF) patients who were admitted in Khon Kaen Hospital. Factors included signs and symptoms before and during admission in hospital, demographic, socio-economic factors of patients and caregivers. The data were collected from interviewing dengue patients and caregivers, and retrieving from medical records. This chapter described the methodology of this study. It included research design, research site, study population, inclusion criteria, exclusion criteria, sample size calculate, methods of data collection and ethical issues.

#### **3.1 Research Design**

The hospital-based case-control study was conducted among dengue patients who were admitted in Khon Kaen Hospital, Khon Kaen province, Thailand.

#### **3.2 Research Site**

The study was carried out at the in-patient department, Khon Kaen Hospital, Khon Kaen province, Thailand. Khon Kaen Hospital was a regional hospital with well medical equipment and health personnel for patients' referral system.

#### **3.3 Study Population**

All dengue patients confirmed by serological test of having DF and DHF admitted in Khon Kaen Hospital from 2 June, 2007 to 2 November, 2007 were included.

**Cases** were all dengue patients who developed DSS diagnosed by physicians and ICD 10 code of DSS = A913 or A914.

**Controls** were all dengue patients who did not develop DSS diagnosed by physicians and ICD 10 code of DF = A90 and DHF = A91.

### **3.4 Inclusion Criteria**

1. Patients who were diagnosed of having serological test of having DF and DHF
2. Patients who were diagnosed of having and not having DSS by physicians
3. Patients admitted at Khon Kaen Hospital during June to November 2007
4. Patients whose parents or/and caregivers agreed to participate under informed consent

### **3.5 Exclusion Criteria**

1. Patients who were unable to respond to interviewing physically and mentally
2. Patients who had incomplete information of factors under study from the medical records

### **3.6 Study Period**

Data collection was performed for the duration of 5 months from 2 June to 2 November 2007.

### **3.7 Sample Size**

The following formula was used for calculating sample size (74).

$$n = \frac{\left( z_{1-\alpha/2} \sqrt{2p(1-p)} + z_{1-\beta} \sqrt{p_1(1-p_1) + p_0(1-p_0)} \right)^2}{(p_1 - p_0)^2}$$

with  $p_1 = \frac{OR_{(p_0)}}{OR_{(p_0)-(1-p_0)}}$  and  $p = \frac{(p_1 + p_0)}{2}$

Signs and symptoms of DSS, especially bleeding was the major interest of this study, and was used as risk factors to estimate sample size. From other study odds ratio of bleeding was 5.1 (61), and bleeding rate among dengue patients without DSS ( $p_0$ ) was 50% (75).

Level of significance was 5%	= 1.96
Power of the test (1 - $\beta$ ) was 90%	= 1.28
Bleeding rate among non DSS ( $p_0$ )	0.50
Odds ratio of bleeding	5.1
Bleeding rate among DSS ( $p_1$ )	0.84
Ratio among cases: controls = 1:3	
Therefore, the minimum sample sizes were	Cases = 30
	Control = 90
	Total = 120

### 3.8 Methods of Data Collection

3.8.1 Data collection from was constructed by the Researcher.

3.8.2 The data were collected by the following methods:

1) A questionnaire developed by Kongsin, et al. (Measurement of dengue burden in Khon Kaen, Thailand: Impact on household of dengue hospitalization) was used for interviewing patients who were admitted in hospital or/and caregivers of study subjects at Khon Kaen Hospital.

2) Clinical data developed by Kongsin, et al. (Measurement of dengue burden in Khon Kaen, Thailand: Impact on household of dengue hospitalization) were retrieved from medical records.

3.8.3 Ethical review and permission of director of hospital was highly concerned.

3.8.4 The detail of information for data collection was the following:

Part I: Demographic data and Socio-economic data of patients

Patients: age, sex, weight, height, education, occupation, residency

Part II: Demographic data and Socio-economic data of caregivers

Caregivers: age, sex, education, occupation, household's income, household's expenditure

Part III: Clinical data before admission in Khon Kaen Hospital

a) Duration of fever before hospitalization

b) Symptoms before admission in Khon Kaen Hospital: vomiting, dizziness, excessive thirst, headache, myalgia, eye pain, bleeding, abdominal pain, etc.

Part IV: Clinical data during admission in Khon Kaen Hospital

a) History of illness with DHF, history of chronic disease (Diabetes mellitus, Hypertension, Renal insufficiency, Thalassemia, G-6-PD deficiency)

b) Signs and symptoms during admission at Khon Kaen Hospital: plasma leakage, headache, anorexia, nausea/vomiting, myalgia, retro-orbital pain, abdominal pain, gum bleeding, epistaxis, GI bleeding (hematemesis, melena, etc.)

c) Laboratory findings: hematocrit (Hct.), white blood cell count (WBC) and platelet counts.

The contents of data collection and questionnaire were reviewed by professionals in DHF and director of hospital.

### **3.9 Access and Ethical Approval**

Protocol of the study was reviewed by the Ethical Review Committee, Mahidol University and the ethical committee of Khon Kaen Hospital. Prior to the process of data collection, written information sheets about the research project were given to participants along with verbal information. After they were permitted to take part in the study, written informed consent form was given to participants for their signature.

### 3.10 Data Analysis

All the analyses were calculated using the computer statistical package and a probability value of the  $p < 0.05$  was considered to be a significant association.

#### 1. Descriptive statistics

All the data of this study were summarized as frequency and percent for categorical variables and mean and standard deviation for the continuous variables. The variables in this study were the demographic characteristics, socio-economic data, clinical data (signs and symptoms) and laboratory investigations.

#### 2. Analytic statistics

Chi-square test and Fisher's exact test to demonstrate the association between factor and DSS.

Univariate analysis was used for crude associated between factors and DSS by RR and 95% confidence intervals (CI).

Binary logistic regression analyses with adjusted RR and 95% intervals (CI) were calculated to demonstrate the association between factors and as dependent variables DSS by using enter method.

## CHAPTER 4

### RESULTS

This chapter presented the results of the study according to objectives of this study which was aimed to find the relationships between clinical manifestation factors, socio-demographic factors and the development of Dengue Shock Syndrome (DSS) among patients admitted with dengue fever in Khon Kaen Hospital, Thailand during June 2 to November 2, 2007.

Overall, 238 cases had been diagnosed to have dengue at admission and had been recruited into the study. However, 23 (10 %) of 238 cases had been confirmed using clinical and laboratory information to have non dengue illness, so the remained 215 cases were included in the analyses (Table 1).

**Table 1** Diagnoses of participants when discharge from hospital

Diagnosis	Number	(%)
Non-dengue illness	23	9.7
Dengue Fever	88	37.0
Dengue Hemorrhagic Fever	90	37.8
Dengue Shock Syndrome	37	15.5
<b>Total</b>	238	100.0
<b>Status of participants</b>		
Dengue Shock Syndrome group	37	17.2
Non Dengue Shock Syndrome group	178	82.8
<b>Total</b>	215	100.0

The results of study were presented as follows:

4.1 Demographic, socio-demographic and clinical characteristics by DSS and non DSS

4.2 The crude associations between related factors to DSS

4.3 The adjusted association between related factors to DSS

## 4.1 Demographic, Socio-economic and Clinical Characteristics

### 4.1.1 Demographic and socio-economic characteristics of study population

Results showed that about half of the patients were male. There was no statistical difference in proportion of sex between DSS group and non DSS group. The proportion of study population with age less than 10 years old among DSS group was about half of non DSS group with statistical significance in proportion by age. Nearly all of DSS group and about 40% of non DSS group lived in the rural area with statistically significant difference in proportion by residential area. Most of dengue patients were not working to earn money (Tables 2 and 3).

**Table 2** Demographic and socio-economic characteristics of dengue patients in Khon Kaen Hospital

Demographic and socio-economic characteristics	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Sex of patients</b>							
Male	109	50.7	21	56.8	88	49.4	0.418
Female	106	49.3	16	43.2	90	50.6	
<b>Total</b>	215	100.0	37	100.0	178	100.0	
Sex ratio (Male : Female)	1.03 : 1		1.31 : 1		0.98 : 1		
<b>Age of Patients (years)</b>							
<10	73	34.0	20	54.1	53	29.8	0.005*
≥ 10	142	66.0	17	45.9	125	70.2	
<b>Total</b>	215	100.0	37	45.9	178	70.2	
Mean age (SD)	11.0	(5.5)	9.3	(4.3)	12	(5.5)	
Min, Max	0.8, 48		4, 27		0.8, 48		
Median			9.0		12.0		

**Table 2** Demographic and socio-economic characteristics of dengue patients in Khon Kaen Hospital (cont.)

Demographic and socio-economic characteristics	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Education</b>							
Studying	169	78.6	26	70.3	143	80.3	0.957
Completed	23	10.7	4	10.8	19	10.7	
No formal education	23	10.7	7	18.9	16	9.0	
<b>Total</b>	215	100.0	37	100.0	178	100.0	
<b>Education (studying)</b>							
Primary school	105	62.1	24	92.3	81	56.6	<0.001*
> primary school	64	37.9	2	7.7	62	43.4	
<b>Total</b>	169	100.0	26	100.0	143	100.0	
<b>Education (complete)</b>							
Primary school	6	26.1	1	25.0	5	26.3	0.957
> primary school	17	73.9	3	75.0	14	73.7	
<b>Total</b>	23	100.0	4	100.0	19	100.0	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value &lt; 0.05

**Table 3** Residency and occupation of dengue patients in Khon Kaen Hospital

Demographic and socio-economic characteristics	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Residency</b>							
Urban	111	51.6	1	2.7	110	61.8	<0.001*
Rural	104	48.1	36	97.3	68	38.2	
<b>Total</b>	215	100.0	37	100.0	178	100.0	
<b>Occupation</b>							
Government employee	1	0.5	0	0.0	1	0.6	0.835
Employee	4	1.9	0	0.0	4	2.3	
Self-employed/merchant	4	1.9	1	2.7	3	1.7	

**Table 3** Residency and occupation of dengue patients in Khon Kaen Hospital (cont.)

Demographic and socio-economic characteristics	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
Agriculture	3	1.4	0	0.0	3	1.7	
Non-government employee	1	0.5	0	0.0	1	0.6	
Not working for pay	201	93.9	36	97.3	165	93.2	
<b>Total</b>	214	100.0	37	100.0	177	100.0	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value < 0.05

#### 4.1.2 Nutrition status of study population

The nutrition status of 167 dengue patients in age group 0-18 years was measured by growth chart. It was found that about 71% and 69% of patients were in normal nutritional status for DSS group and non DSS group, respectively. About 16% and 13% were thin and fat respectively in DSS group. About 24% and 7% were thin and fat respectively in non DSS group. There was no statistical significance in proportion of nutritional status among these two groups of DSS and non DSS (p-value = 0.363) (Table 4).

For the body mass index (BMI) of 18 dengue patients in age group  $\geq 18$  years old, it was found that among DSS group there was only one patient with normal BMI. Among non DSS group, there 47%, 29% and 12% of patients were in normal, underweight, at risk overweight or obesity I, respectively. BMI of patient did not demonstrate statistically significance (p-value = 0.787) (Table 4).

**Table 4** Nutritional status of dengue patients in Khon Kaen Hospital

Nutritional Status	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Age 0-18 years old</b>							
Thin	38	22.8	5	16.1	33	24.3	0.363
Normal	116	69.5	22	71.0	94	69.1	
Fat	13	7.8	4	12.9	9	6.6	
<b>Total</b>	167	100.0	31	100.0	136	100.0	
<b>Age &gt; 18 years old</b>							
Underweight (Below 18.5)	5	29.4	0	0.0	5	29.4	0.787
Normal (18.5 – 22.9)	9	47.1	1	100.0	8	47.1	
At risk overweight (23 – 24.9)	2	11.8	0	0.0	2	11.8	
Obesity I (25 – 29.9)	2	11.8	0	0.0	2	11.8	
Obesity II ( $\geq 30$ )	0	0.0	0	0.0	0	0.0	
<b>Total</b>	18	100.0	1	100.0	17	100.0	

<sup>a</sup> Pearson's chi-square test

#### 4.1.3 The demographic and socio-economic characteristics of caregivers

Among the total number of 200 caregivers of dengue patients, 54% and 61% of them were mothers of dengue patients in DSS group and non DSS group, respectively. The average age of caregivers was about 42 years old in both dengue with shock group and dengue without shock group. The most of caregivers of DSS group and non DSS group were female (89.2% and 85.9% respectively). Most of caregivers of DSS group and non DSS group finished primary school (80.6% and 71.5% respectively) (Table 5).

**Table 5** Demographic characteristics of caregivers in Khon Kaen Hospital

Caregiver characteristics	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Caregiver</b>							
Mother	120	60	20	54.1	100	61.3	0.252
Father	18	9	2	5.4	16	9.8	
Grandmother	35	17.5	11	29.7	24	14.7	
Grandfather	9	4.5	1	2.7	8	4.9	
Older, younger brother or sister of patients	2	1.0	0	0.0	2	1.2	
Aunt-Uncle	10	5.0	3	8.1	7	4.3	
Husband-Wife and friend	6	3.0	0	0.0	6	3.7	
<b>Total</b>	200	100.0	37	100.0	167	100.0	
<b>Sex of caregivers</b>							
Male	27	13.5	4	10.8	23	14.1	0.596
Female	173	86.5	33	89.2	140	85.9	
<b>Total</b>	200	100.0	37	100.0	163	100.0	
<b>Age</b>							
Mean (SD)	42.0	(40.0)	42.0	(10.0)	42.1	(10.9)	
Min(Max)	16	76	28	(68)	16	(76)	
Median	40		39		41		
<b>Education</b>							
Studying	3	1.5	0	0.0	3	1.8	0.571
Finished studying	194	97.0	36	97.3	158	96.9	
No formal education	3	1.5	1	2.7	2	1.2	
<b>Total</b>	200	100.0	37	100.0	163	100.0	
<b>Education (complete)</b>							
Primary school	142	73.2	29	80.6	113	71.5	0.269
> Primary school	52	26.8	7	19.4	45	28.5	
<b>Total</b>	194	100.0	36	100.0	158	100.0	

<sup>a</sup> Pearson's chi-square test

The occupation of about 40.5% of caregivers of DSS group was in agriculture, 27% working with no payment and 16.2% were employees. For the caregivers of non DSS group, their occupation was 27.6% was in agriculture, 23.3% were working with no payment. There were no significant difference in proportions of occupation between the two groups ( $p$ -value = 0.495) (Table 6).

The average household's income per month in DSS group was 6,352.6±7,248.5 baht and among non DSS group was 12,901.1±25,064.5 baht. The proportion of caregivers with income of household per month  $\leq$  6,000 baht was 75%, while in non DSS group was 45.3%. There was statistically significant difference household's income in the two groups ( $p$ -value = 0.001) (Table 6).

The average household's expenditure per month among caregivers in DSS group was lower than those among the non DSS group. Proportion of caregivers with household's expenditure  $>$  5000 baht among DSS group was higher than those of the non DSS group with statistically significantly difference ( $p$ -value = 0.003) (Table 6).

**Table 6** Socio-economic characteristics of caregivers in Khon Kaen Hospital

Caregiver characteristics	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Occupation</b>							
Government employee	12	6.0	2	5.4	10	6.1	0.495
Employee	40	20.0	6	16.2	34	20.9	
Self-employed/merchant	26	13.0	2	5.4	24	14.7	
Agriculture	60	30.0	15	40.5	45	27.6	
Non-government employee	14	7.0	2	5.4	12	7.4	
Working with no payment	48	24.0	10	27.0	38	23.3	
<b>Total</b>	200	100.0	37	100.0	163	100.0	
<b>Household's Income per Month</b>							
Mean (SD)	11,632.1	(22,364.2)	6,352.6	(7,248.5)	12,901.0	(25,064.5)	
Min(Max)	983.0	(300,000.0)	1,000.0	(40,000.0)	983.0	(300,000.0)	
≤ 6,000.0 Baht	100	50.8	27	75.0	73	45.3	0.001*
> 6,000.0 Baht	97	49.2	9	25.0	88	54.7	
<b>Total</b>	197	100.0	36	100.0	161	100.0	
<b>Household's expenditure per Month</b>							
Mean (SD)	8,477.4	(10,301.1)	5,125.3	(4,082.1)	9,146.7	(11,008.2)	
Min(Max)	1,000.0	(100,000.0)	1,000.0	(25,000.0)	1,500.0	(100,000.0)	
≤ 5,000.0 Baht	93	47.2	9	25.0	84	52.2	
> 5,000.0 Baht	104	52.8	27	75.0	77	47.8	0.003*
<b>Total</b>	197	100.0	36	100.0	161	100.0	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value < 0.05

#### 4.1.4 The clinical data of dengue patients before and during admission in hospital

##### 4.1.4.1 Duration of fever

The average duration of fever before admitted in Khon Kaen Hospital in DSS group and non DSS group was  $4.7 \pm 1.1$  days and  $3.8 \pm 1.5$  days, respectively with statistically significance of means ( $p$ -value < 0.001). Proportions of patients with longer duration > 4 days of having fever before admission in hospital among non DSS was higher than DSS group with statistical significant difference ( $p$ -value < 0.001) (Table 7).

After admission in hospital, the average durations of having fever were lower. Means duration of fever among DSS group was  $0.9 \pm 1.6$  days and among non DSS group was  $1.3 \pm 1.2$  days with statistically significance of means among the two groups ( $p$ -value = 0.013). There was no difference in proportions of the two groups of patients by the duration of having fever > 1 days after admission in hospital ( $p$ -value = 0.960) (Table 7).

**Table 7** Duration of fever before and during admission in hospital among study Participants

Duration of fever	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Before admission</b>							
Mean (SD)	3.9	(1.5)	4.7	(1.1)	3.8	(1.5)	<0.001**
Min, Max	0	8.0	2.0	6.0	0	8.0	
Median	4.0		5.0		4.0		
0 - 4 days	76	35.3	27	73.0	49	27.5	<0.001*
5 - 8 days	139	64.7	10	27.0	129	72.5	
<b>Total</b>	215	100.0	37	100.0	178	100.0	
<b>During admission</b>							
Mean (SD)	1.3	(1.3)	0.9	(1.6)	1.3	(1.2)	0.013**
Min, Max	0	8.0	0	8.0	0	5.0	
Median	1.0		0		1.0		
1 day	60	43.2	7	43.8	53	43.1	0.960
2-8 days	79	56.8	9	56.3	70	56.9	
<b>Total</b>	139	100.0	16	100.0	123	100.0	

<sup>a</sup> p-value from Mann-Whitney U test

\* Significant at  $p$ -value < 0.05

#### 4.1.4.2 Underlying diseases

Most of patients in DSS group and non DSS group had no underlying diseases. Two cases had diabetes mellitus in non DSS group, 1 case had Thalassemia in DSS group. Both DSS group and non DSS group had one case of G - 6 - PD deficiency with no statistically significance ( $p$ -value = 0.563, 0.517, 0.172 and 0.217, respectively) (Table 8).

**Table 8** Underlying diseases of study population

Underlying diseases	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Having history of illness</b>							
<b>with dengue before</b>							
Yes	13	6.0	3	8.1	10	5.6	0.563
No	202	94.0	34	91.9	168	94.4	
<b>Diabetes mellitus</b>							
Yes	2	0.9	0	0.0	2	1.1	0.517
No	213	99.1	37	100.0	176	98.9	
<b>Hypertension</b>							
Yes	0	0.0	0	0.0	0	0.0	**N/A
No	215	100.0	37	100.0	178	100.0	
<b>Renal insufficiency</b>							
Yes	0	0.0	0	0.0	0	0.0	**N/A
No	215	100.0	37	100.0	178	100.0	
<b>Thalassemia</b>							
Yes	1	0.5	1	2.7	0	0.0	0.172
No	214	99.5	36	97.3	178	100.0	
<b>G - 6 -PD deficiency</b>							
Yes	2	0.9	1	2.7	1	0.6	0.217
No	213	99.1	36	97.3	177	99.4	

<sup>a</sup> Pearson's chi-square test

\*\* N/A = Not applicable

#### 4.1.4.3 Symptoms of dengue patients before admitted in hospital

From interviewing the caregivers and patients with and without DSS groups: By the symptoms before admission in Khon Kaen Hospital, it was found that there were higher proportions of patients with vomiting, reducing of urine output, bleeding (small red spots on the skin, spontaneous bruises, nose bleeding, gum bleeding and other bleeding), epigastric/abdominal pain and diarrhea among DSS group compared to non DSS group. But the proportion of patients having dizziness excessive thirst, headache, skin rash, eye pain, muscle/joint pain including sore throat and running was found higher in non DSS group than in DSS group. *There were statistical significant differences in proportions of having muscle/joint pain, bleeding (small red spots on the skin, spontaneous bruises, nose bleeding, gum bleeding and other bleeding), Epigastric/Abdominal pain among DSS and non DSS group (p-value <0.001 and 0.003) (Table 9).*

**Table 9** Symptoms of dengue patients before admitted in Khon Kaen Hospital

Symptoms from interview data	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Vomiting</b>							
Yes	144	67.0	28	75.7	116	65.2	0.216
No	71	33.0	9	24.3	62	34.8	
<b>Dizziness</b>							
Yes	176	81.9	29	78.4	147	82.6	0.546
No	39	18.1	8	21.6	31	17.4	
<b>Excessive thirst</b>							
Yes	80	37.2	9	24.3	71	39.9	0.075
No	135	62.8	28	75.7	107	60.1	
<b>Reduce urine output</b>							
Yes	89	41.4	19	51.4	70	39.3	0.177
No	126	58.6	18	48.6	108	60.7	
<b>Headache</b>							
Yes	177	82.3	28	75.7	149	83.7	0.244
No	38	17.7	9	24.3	29	16.3	

**Table 9** Symptoms of dengue patients before admitted in Khon Kaen Hospital (cont.)

Symptoms from interview data	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Skin rash</b>							
Yes	27	12.6	4	10.8	23	12.9	0.724
No	188	87.4	33	89.2	155	87.1	
<b>Eye pain</b>							
Yes	38	17.7	4	10.8	34	19.1	0.229
No	177	82.3	33	89.2	144	80.9	
<b>Muscle or joint pain</b>							
Yes	159	74.0	21	56.8	138	77.5	0.009*
No	56	26.0	16	43.2	40	22.5	
<b>Bleeding**</b>							
Yes	71	33.0	22	59.5	49	27.5	<0.001*
No	144	67.0	15	40.5	129	72.5	
<b>Epigastric/Abdominal pain</b>							
Yes	121	56.3	29	78.4	92	51.7	0.003*
No	94	43.7	8	21.6	86	48.3	
<b>Diarrhea</b>							
Yes	113	52.6	22	59.5	91	51.1	0.356
No	102	47.4	15	40.5	87	48.9	
<b>Sore throat</b>							
Yes	97	45.1	14	37.8	83	46.6	0.328
No	118	54.9	23	62.2	95	53.4	
<b>Running nose</b>							
Yes	38	17.7	5	13.5	33	18.5	0.466
No	177	82.3	32	86.5	145	81.5	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value &lt; 0.05

\*\* Bleeding = small red spots on the skin, spontaneous bruises, nose bleeding, gum bleeding and other bleeding

### 4.1.5 Clinical manifestations of patients during admitted in Khon Kaen Hospital

#### 4.1.5.1 Symptoms

There were higher proportion of patients with epigastric pain (81.1%) in the DSS group than in the non DSS group (57.3%) with statistical significance (p-value = 0.007). But proportions of patients with retro-orbital pain (16.3%), myalgia/arthralgia (56.2%) were higher in non DSS group than in the DSS group (2.7% and 43.2% respectively) with statistical significance (p-value = 0.03 and 0.009). Other sign and symptoms did not demonstrate significant difference in proportions between the two groups (Table 10).

**Table 10** Symptoms of dengue patients during admission in Khon Kaen Hospital

Symptoms	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Headache</b>							
Yes	121	56.3	18	48.6	103	57.9	0.304
No	94	43.7	19	51.4	75	42.1	
<b>Retro – orbital pain</b>							
Yes	30	14.0	1	2.7	29	16.3	0.030*
No	185	86.0	36	97.3	149	80.7	
<b>Myalgia/arthralgia</b>							
Yes	116	54.0	16	43.2	100	56.2	0.009*
No	99	46.0	21	56.8	78	43.8	
<b>Anorexia</b>							
Yes	188	87.4	32	86.5	156	87.6	0.847
No	27	12.6	5	13.5	22	12.4	
<b>Rash</b>							
Yes	139	64.7	22	59.5	117	65.7	0.468
No	76	45.3	15	40.5	61	34.3	
<b>Vomiting</b>							
Yes	91	42.3	18	48.6	73	41.0	0.392
No	124	57.7	19	51.4	105	59.0	

**Table 10** Symptoms of dengue patients during admission in Khon Kaen Hospital (cont.)

Symptoms	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Epigastric pain</b>							
Yes	132	61.4	30	81.1	102	57.3	0.007*
No	83	38.6	7	18.9	76	42.7	
<b>Excessive thirst</b>							
Yes	93	43.3	12	32.4	81	45.5	0.144
No	122	56.7	25	67.6	97	54.5	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value &lt; 0.05

#### 4.1.5.2 Hemorrhagic manifestations

Most of these patients had experience with any types of hemorrhagic manifestations both in DSS group and non DSS group. The significant differences in proportions found in epistaxis, gum bleeding and hematemesis/melena with higher proportions in DSS group (p-value = 0.04, 0.004 and <0.001, respectively). Others did not demonstrate significant differences (Table 11).

**Table 11** Hemorrhagic manifestations of dengue patients during admitted in Khon Kaen Hospital

Hemorrhagic manifestations	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Having any experienced in hemorrhagic manifestations</b>							
Yes	189	87.9	33	89.2	156	87.6	0.793
No	26	12.1	4	10.8	22	12.4	
<b>Positive tourniquet test</b>							
Yes	151	70.2	23	62.2	128	71.9	0.238
No	64	29.8	14	37.8	50	28.1	
<b>Petechiae</b>							
Yes	100	46.5	16	43.2	84	47.2	0.661
No	115	53.5	21	56.8	94	52.8	

**Table 11** Hemorrhagic manifestations of dengue patients during admitted in Khon Kaen Hospital (cont.)

Hemorrhagic manifestations	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Purpura</b>							
Yes	0	0.0	0	0.0	0	0.0	N/A
No	215	100.0	37	100.0	178	100.0	
<b>Echymosis</b>							
Yes	2	0.9	1	2.7	1	0.6	0.217
No	213	99.1	36	97.3	177	99.4	
<b>Epistaxis</b>							
Yes	48	22.3	13	35.1	35	19.7	0.040*
No	167	77.7	24	64.9	143	80.3	
<b>Gum bleeding</b>							
Yes	44	20.5	14	37.8	30	16.9	0.004*
No	171	79.5	23	62.2	148	83.1	
<b>Hematemesis/melena</b>							
Yes	69	32.1	22	59.5	47	26.4	<0.001*
No	146	67.9	15	40.5	131	73.6	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value &lt; 0.05

#### 4.1.5.3 Plasma leak, ascites, abdominal pain and liver enlargement

From medical records in hospital, it was found that dengue patients with DSS had significant higher proportions of having all signs and symptoms related closely to shock syndrome. All of patients belonged to DSS group had clinical evidence of plasma leak, while the non DSS group had plasma leak by 53.4%. Proportion of having pleural effusion by clinical diagnosis found 51.4% in DSS group when non DSS group was only 13.5% (p-value<0.001). Higher proportions of having ascites, abdominal pain and enlargement of liver also found among patients with DDS group compared to non DSS group (p-value <0.001, 0.043 and <0.001, respectively) (Table 12).

**Table 12** Signs of plasma leak of dengue patients during admitted in Khon Kaen Hospital

Signs of plasma leak	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Having clinical evidence of plasma leak</b>							
Yes	132	61.4	37	100.0	95	53.4	<0.001*
No	83	38.6	0	0.0	83	46.6	
<b>Pleural effusion (clinically diagnosed)</b>							
Yes	43	20.0	19	51.4	24	13.5	<0.001*
No	172	80.0	18	48.6	154	86.5	
<b>Ascites (clinically diagnosed)</b>							
Yes	30	14.0	16	43.2	14	7.9	<0.001*
No	185	86.0	21	56.8	164	92.1	
<b>Abdominal pain (clinically diagnosed)</b>							
Yes	79	36.7	19	51.4	60	33.7	0.043*
No	136	63.3	18	48.6	118	66.3	
<b>Enlargement of liver (clinically diagnosed)</b>							
Yes	96	44.7	29	78.4	67	37.6	<0.001*
No	119	55.3	8	21.6	111	62.4	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value &lt; 0.05

#### 4.1.5.4 Hypoperfusion

Most of dengue patients with shock group had proportions of clinical evidences of having hypoperfusion, narrow pulse pressure or small volume pulse volume, cold extremities, lethargy, slow capillary relief, clammy skin, lethargy, restlessness including oliguria compared to patients in non DSS group who mostly did not have (p-value<0.001) (Table 13).

**Table 13** Signs and symptoms of hypoperfusion of dengue patients during admitted in Khon Kaen Hospital

Signs and symptoms of hypoperfusion	Total (n = 215)		DSS (n = 37)		Non DSS (n = 178)		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Did the patient have clinical evidence of hypoperfusion</b>							
Yes	33	15.3	32	86.5	0	0	
No	183	84.7	5	13.5	178	100.0	<0.001*
<b>Narrow pulse pressure or small pulse volume</b>							
Yes	35	16.3	35	94.6	0	0	
No	180	83.7	2	5.4	178	100.0	<0.001*
<b>Cold extremities</b>							
Yes	30	14.9	30	81.1	0	0	
No	185	85.1	7	18.9	178	100.0	<0.001*
<b>Slow capillary relief</b>							
Yes	24	11.6	24	64.9	0	0	
No	191	88.4	13	35.1	178	100.0	<0.001*
<b>Clammy skin</b>							
Yes	24	11.6	24	64.9	0	0	
No	191	88.4	13	35.1	178	100.0	<0.001*
<b>Lethargy</b>							
Yes	141	65.6	34	91.9	107	60.1	<0.001*
No	74	34.4	3	8.1	71	39.9	
<b>Restlessness</b>							
Yes	49	22.8	31	83.8	18	10.1	<0.001*
No	166	77.2	6	16.2	160	89.9	
<b>Oliguria</b>							
Yes	28	13.5	28	75.7	0	0	<0.001*
No	187	86.5	9	24.3	178	100.0	

<sup>a</sup> Pearson's chi-square test

\* Significant at p-value &lt; 0.05

#### 4.1.5.5 Laboratory results

Most of DSS group (94.6%) were referred from other hospitals nearby. It was found that all patients in DSS group had hematocrit increased  $\geq 20\%$ , platelet counts  $< 100,000$  cells/mm<sup>3</sup> (94.4%), and white blood cell counts  $< 5,000$  cells/mm<sup>3</sup> (72.2%) higher than in the non DSS group (51.7%, 61.8% and 13.6% respectively) significantly (p-value $<0.001$ , 0.036 and 0.001, respectively) (Table 14).

**Table 14** Results of Laboratory testes of dengue patients during admitted in Khon Kaen Hospital

Laboratory data	Total		DSS		Non DSS		P-value <sup>a</sup>
	No.	%	No.	%	No.	%	
<b>Hematocrit Final interprets</b>	n = 215		n = 37		n = 178		
Increase $\geq 20\%$	129	60.0	37	100.0	92	51.7	$<0.001^*$
Increase $< 20\%$	86	40.0	0	0.0	86	48.3	
<b>Final interpreted of platelet counts</b>	n = 206		n = 36		n = 170		
$< 100,000$ cell/mm <sup>3</sup>	139	67.5	34	94.4	105	61.8	$<0.001^*$
$\geq 100,000$ cell/ mm <sup>3</sup>	67	32.5	2	5.6	65	38.2	
<b>WBC</b>	n = 205		n = 36		n = 169		
$< 5,000$ cell/ mm <sup>3</sup>	172	83.9	26	72.2	146	86.4	0.036*
$\geq 5,000$ cell/ mm <sup>3</sup>	33	16.1	10	27.8	23	13.6	
<b>Case referred</b>	n = 215		n = 37		n = 178		
Yes	99	46.0	35	94.6	64	36.0	$<0.001^*$
No	116	54.0	2	5.4	114	64.0	

<sup>a</sup> Pearson’s chi-square test

\* Significant at p-value  $< 0.05$

## 4.2 Crude Associations between Factors and DSS by Univariate Analysis

### 4.2.1 Demographic and socio-economic characteristics of dengue patients

Age, education (studying) and residential area of dengue patients had significant associations with dengue with shock (DSS). The dengue patients with age  $< 10$

years old had 2.78 times higher risk to develop DSS than patients with age  $\geq 10$  years (OR = 2.78, 95% CI = 1.35 – 5.72). The risk to develop DSS among patients who were studying primary school was 9.19 times higher than those who were studying higher than primary school (OR = 9.19, 95%CI = 2.09 – 40.34). And dengue patients who were living in rural area had higher risk to develop DSS than those who were living in urban area (OR = 58.34, 95% CI = 7.80 – 434.57) (Table 15).

**Table 15** Crude odds ratio for DSS by demographic and socio-economic characteristics of dengue patients

Demographic and socio-economic characteristics	DSS		Non DSS		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Age of patients, years</b>	n = 37		n = 178				
$\geq 10$ years <sup>#</sup>	17	45.9	125	70.2	1.00		
<10 years	20	54.1	53	29.8	2.78	1.35 – 5.72	0.005
<b>Education (Studying)</b>	n = 26		n = 143				
> Primary <sup>#</sup> school	2	7.7	62	43.4	1.00		
Primary school	24	92.3	81	56.6	9.19	2.09 – 40.34	0.001
<b>Residency</b>	n = 37		n = 178				
Urban <sup>#</sup>	1	2.7	110	61.8	1.00		
Rural	36	97.3	68	38.2	58.34	7.80 – 434.57	<0.001

# Reference group

\* p-value from chi-square test

#### 4.2.2 Socio-economic characteristics of caregivers

Monthly household's income and household's expenditure (baht/month) showed a significant risk of having DSS. It was found that those who had household's income less than 6,000 baht/month had 3.62 times higher risk of DSS when compared to those who had household's income more than 6,000 baht/month (OR = 3.62, 95%CI = 1.60 – 8.18) (Table 16).

The caregivers who had the household's expenditure more than 5,000 baht/month had 3.27 times higher risk of DSS when compared to those who had household's expenditure less than 5,000 baht (OR = 3.27, 95%CI = 1.45 – 7.40) (Table 16).

**Table 16** Crude odds ratio DSS by socio-economic status of dengue patients' caregivers

Socio-economic data	DSS (n = 36)		Non DSS (n=161)		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Household's income/ Month</b>							
> 6,000 Baht <sup>#</sup>	9	25.0	88	54.7	1.00		
≤ 6,000 Baht	27	75.0	73	45.3	3.62	1.60 – 8.18	0.001
<b>Household's expenditure/Month</b>							
≤5,000 Baht <sup>#</sup>	9	25.0	84	52.2	1.00		
>5,000 Baht	27	75.0	77	47.8	3.27	1.45 – 7.40	0.003

# Reference group

\* p-value from chi-square test

#### 4.2.3 Duration of having fever before admission in hospital

The dengue patients whose duration of fever before hospitalization within 5-8 days had 7.11 times higher risk to develop DSS than those who had the duration of fever before hospitalization equal and less than 4 days (OR = 7.11, 95%CI = 3.21 – 15.77) (Table 17).

**Table 17** Crude odds ratio for DSS by duration of fever before admission in Khon Kaen Hospital

Clinical data	DSS (n = 37)		Non DSS (n=178)		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Duration of fever before hospitalization</b>							
0 - 4 days <sup>#</sup>	27	73.0	49	27.5	1.00		
5 - 8 days	10	27.0	129	72.5	7.11	3.21 – 15.77	<0.001

# Reference group

\* p-value from chi-square test

#### 4.2.4 Symptoms before admission in hospital

Symptom from interviewing dengue patients showed that patients who did not have muscle or joint pain had higher risk to develop DSS 2.63 times than who had muscle or joint pain (OR = 2.63, 95%CI = 1.26 – 5.51). Dengue patients who had

bleeding and abdominal pain had risk 3.86 times and 3.39 times higher than who did not have bleeding and abdominal pain (OR = 3.86, 95%CI = 1.86 - 8.05 and OR = 3.39, 95%CI = 1.47 - 7.82) (Table 18).

**Table 18** Crude odds ratio for DSS by symptoms before admission in hospital

Symptoms from interview data	DSS (n = 37)		Non DSS (n=178)		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Muscle or joint pain</b>							
Yes #	21	56.8	138	77.5	1.00		
No	16	43.2	40	22.5	2.63	1.26 – 5.51	0.009
<b>Bleeding</b>							
Yes #	15	40.5	129	72.5	1.00		
No	22	59.5	49	27.5	3.86	1.86 - 8.05	<0.001
<b>Abdominal pain</b>							
Yes #	8	21.6	86	48.3	1.00		
No	29	78.4	92	51.7	3.39	1.47 – 7.82	0.003

# Reference group

\* p-value from chi-square test

#### 4.2.5 Other symptoms during admission in hospital

The results showed that the dengue patients who had episgatic pain, epistaxis, gum bleeding and hematemesis or melena had higher risk to develop DSS 3.19, 2.21, 3.00 and 4.09 times respectively when compared to those who did not have episgatic pain, epistaxis, gum bleeding and hematemesis or melena with statistical significances (OR = 3.19, 95%CI = 1.33 – 7.66), (OR = 2.21, 95%CI = 1.03 – 4.78), (OR = 3.00, 95%CI = 1.39 – 6.50) and (OR = 4.09, 95%CI = 1.96 – 8.53), respectively (Table 19).

**Table 19** Crude odds ratio for DSS by symptoms of dengue patients during admission in hospital

Symptoms	DSS (n = 37)		Non DSS (n=178)		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Epigastric pain</b>							
Yes #	7	18.9	76	42.7	1.00		
No	30	81.1	102	57.3	3.19	1.33 – 7.66	0.007
<b>Epistaxis</b>							
Yes #	24	64.9	143	80.3	1.00		
No	13	35.1	35	19.7	2.21	1.03 – 4.78	0.040
<b>Gum bleeding</b>							
Yes #	23	62.2	148	83.1	1.00		
No	14	37.8	30	16.9	3.00	1.39 – 6.50	0.040
<b>Hematemesis/melena</b>							
Yes #	15	40.5	131	73.6	1.00		
No	22	59.5	47	26.4	4.09	1.96 – 8.53	<0.001

# Reference group

\* p-value from chi-square test

#### 4.2.6 Plasma leak

Dengue patients who had pleural effusion, abdominal distension, enlargement of liver and ascites had significantly higher risk to develop DSS compared to those who did not have pleural effusion, abdominal distension, enlargement of liver and ascites (OR = 6.77, 95%CI = 3.12 – 14.70), (OR = 2.08, 95%CI = 1.02 – 4.25), (OR = 6.01, 95%CI = 2.59 – 13.90) and (OR = 8.93, 95%CI = 3.82 – 20.86), respectively (Table 20).

**Table 20** Crude odds ratio for DSS by signs of plasma leak of dengue patients during admission in hospital

Symptoms of plasma leak	DSS (n = 37)		Non DSS (n=178)		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Pleural effusion</b>							
Yes #	18	48.6	154	86.5	1.00		
No	19	51.4	24	13.5	6.77	3.12 – 14.70	<0.001
<b>Abdominal distension</b>							
Yes #	18	48.6	118	66.3	1.00		
No	19	51.4	60	33.7	2.08	1.02 – 4.25	0.043
<b>Enlargement of liver</b>							
Yes #	8	21.6	111	62.4	1.00		
No	29	78.4	67	37.6	6.01	2.59 – 13.90	<0.001
<b>Ascites</b>							
Yes #	21	56.8	164	92.1	1.00		
No	16	43.2	14	7.9	8.93	3.82 – 20.86	<0.001

# Reference group

\* p-value from chi-square test

#### 4.2.7 Hypoperfusion

Dengue patients with lethargy were found to have 7.52 times the risk to develop DSS compared to those who did not have lethargy. (OR = 7.52, 95%CI = 2.23 – 25.42) (Table 21).

Restlessness in dengue patients produced higher risk 45.93 times to develop DSS when compared to who did not have restlessness (OR = 45.93, 95%CI = 16.88 – 124.94) (Table 21).

**Table 21** Crude odds ratio for DSS by symptoms of hypoperfusion of dengue patients during admission in hospital

Symptoms of hypoperfusion	DSS (n = 37)		Non DSS (n=178)		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Lethargy</b>							
Yes #	3	8.1	71	39.9	1.00		
No	34	91.9	107	60.1	7.52	2.23 – 25.42	<0.001
<b>Restlessness</b>							
Yes #	6	16.2	160	89.9	1.00		
No	31	83.8	18	10.1	45.93	16.88 – 124.94	<0.001

# Reference group

\* p-value from chi-square test

#### 4.2.8 Results from laboratory tests and referred cases

Dengue patients with the final interpretation of platelet counts less than 100,000 cells/mm<sup>3</sup> were more likely to have the higher risk to develop DSS 10.52 times (OR = 10.52, 95%CI = 2.45 – 45.28) compared to those who had higher platelet counts than 100,000 cells/mm<sup>3</sup> (Table 22).

Dengue patients who had white blood cells less than 5,000 cells/mm<sup>3</sup> had 2.44 times higher risk to develop DSS when compared to those who had white blood cell more than 5,000 cells/mm<sup>3</sup> (OR = 2.44 , 95%CI = 1.04 – 5.72) (Table 22).

Dengue patients who were referred from other hospitals had risk 31.17 times to develop DSS when compared to those who was not referred cases (OR = 31.17, 95%CI = 7.26 – 133.86) (Table 22).

**Table 22** Crude odds ratio for DSS by laboratory data and referred cases.

Laboratory data	DSS		Non DSS		OR	95%CI	P-value*
	No.	%	No.	%			
<b>Final interpret of platelet counts</b>	n=36		n=170				
≥ 100,000 cell/mm <sup>3#</sup>	2	5.6	65	38.2	1.00		
< 100,000 cell /mm <sup>3</sup>	34	94.4	105	61.8	10.52	2.45 – 45.28	<0.001
<b>WBC</b>	n=36		n=169				
≥ 5,000 cell/mm <sup>3#</sup>	10	27.8	23	13.6	1.00		
< 5,000 cell/mm <sup>3</sup>	26	72.2	146	86.4	2.44	1.04 – 5.72	0.036
<b>Referred case</b>	n=37		n=178				
No <sup>#</sup>	2	5.4	114	64.0	1.00		
Yes	35	94.6	64	36.0	31.17	7.26 – 133.86	<0.001

# Reference group

\* p-value from chi-square test

### 4.3 The Adjusted Association between Factors and Dengue Shock Syndrome (DSS)

Unconditional binary logistic regression with enter method was used in calculation for adjusted effects and calculated Odds ratio with 95% confident interval.

Detection and removal of non significant variables in model was performed, but non significant variables or factors which were considered to be potential confounders from reviewing of literature still remained in the model. There were 8 factors or variables included in the final model which were sex of patients, age of patients, residential area, signs and symptoms before admission in hospital which were muscle or joint pain, and bleeding and signs and symptom during admission in Hospital which were positive tourniquet test, enlargement of liver and ascites. Final model produced a significant at  $p$ -value < 0.001 from Chi-square test, -2 Log likelihood = 94.76, Nagelkerke R square = 0.632.

There were 7 variables or factors demonstrated significant risk to develop DSS, namely sex of patients, residential area, symptoms before admission in Hospital which were muscle or joint pain, bleeding, positive tourniquet test, during admission

in Hospital which were enlargement of liver and ascites. The interpretation of each adjusted risk was controlling for the effect of other variables in the last model (Table 23).

### **Sex of patients**

In crude analysis, there was no association between sex of patients and DSS. But results from multivariate analysis, significant association of sex and development of DSS was found. Being male had higher risk to develop DSS compared to female (adjusted OR = 7.93, 95%CI = 2.02 – 31.10) (Table 23).

### **Residential area**

The risk of DSS was significant greater in dengue patients, who were living in rural area had higher risk to develop DSS than who were living in urban area (OR = 58.24, 95%CI = 7.80 – 434.57) in crude analysis. After controlling for other potential factors, it was found that dengue patients who were living in rural still had higher risk to develop DSS than those who were living in urban area (adjusted OR = 42.21, 95%CI = 4.92 – 362.32) (Table 23).

### **Muscle or joint pain**

The dengue patients who did not have muscle or joint pain had higher risk to develop DSS 2.63 times than who had muscle or joint pain (OR = 2.63, 95%CI = 1.26 – 5.51). By multivariate analysis those who did not have muscle or joint pain had higher risk to develop DSS 6.77 times than those who had muscle or joint pain (adjusted OR = 6.77, 95%CI = 1.83 – 25.00) (Table 23).

### **Bleeding before admission**

The risk to develop DSS in crude analysis was significantly greater in dengue patients who had bleeding before admission in Khon Kaen Hospital (OR = 3.86, 95%CI = 1.85 – 8.05). After controlling other potential factors by logistic regression analysis, it was found that the risk to have a shock for those who were bleeding prior to admission was 12 times higher than those who were not bleeding before admission (adjusted OR = 12.00, 95%CI = 3.15 – 45.44) (Table 23).

### Positive tourniquet test

In crude analysis, there was no association between negative tourniquet test of patients and DSS. But from the results from multivariate analysis, significant association of negative tourniquet test and development of DSS was found. Being negative tourniquet test had higher risk to develop DSS compared to female (adjusted OR = 5.52, 95%CI = 1.52 – 20.13) (Table 23).

### Enlargement of liver

The risk of DSS was significantly greater in dengue patients. Those who had enlarged liver had higher risk to develop DSS than those who were living in urban (OR = 6.01, 95%CI = 2.59 – 13.90) in crude analysis. After controlling other potential factors, it was found that dengue patients who were having enlargement of liver still had higher risk to develop DSS than those who did not have enlargement of liver (adjusted OR = 3.76, 95%CI = 1.15 – 12.32) (Table 23).

### Ascites during admission

From crude analysis, it was found that dengue patients who were having ascites during admission had significantly higher risk to develop DSS compared to those who did not (OR = 8.93, 95%CI = 3.82 – 20.86). After adjusted for other risk factors in multivariate analysis, risk increased to DSS (adjusted OR = 7.83, 95%CI = 2.16 – 28.37) (Table 23).

**Table 23** Crude and Adjusted odds ratio of DSS by factors

Variables	Crude		Adjusted		p-value*
	OR	95% CI	OR	95% CI	
<b>Sex of patients</b>					
Female <sup>#</sup>	1.00		1.00		
Male	1.34	0.66 – 2.74	7.93	2.02 – 31.10	0.003
<b>Age of patients</b>	0.87	0.80 – 1.00	0.90	0.79 – 1.02	0.102
<b>Residency</b>					
Urban <sup>#</sup>	1.00		1.00		
Rural	58.24	7.80 – 434.57	42.21	4.92 – 362.32	0.001

**Table 23** Crude and Adjusted odds ratio of DSS by factors (cont.)

Variables	Crude		Adjusted		<i>p</i> -value*
	OR	95% CI	OR	95% CI	
<b>Muscle or joint pain</b>					
Yes #	1.00		1.00		
No	2.63	1.26 – 5.51	6.77	1.83 – 25.00	0.004
<b>Bleeding before admission</b>					
No#	1.00		1.00		
Yes	3.86	1.85 – 8.05	12.00	3.15 – 45.44	<0.001
<b>Positive Tourniquet Test</b>					
Yes #	1.00		1.00		
No	1.56	0.76 – 3.27	5.52	1.52 – 20.13	0.01
<b>Enlargement of liver</b>					
No#	1.00		1.00		
Yes	6.01	2.59 – 13.90	3.76	1.15 – 12.32	0.029
<b>Ascites during admission</b>					
No#	1.00		1.00		
Yes	8.93	3.82 – 20.86	7.83	2.16 – 28.37	0.002

# Reference group

\* *p*-value from Wald statistic

\*\* one variable adjusted for all other variables in the table

## CHAPTER 5

### DISCUSSION

This study was conducted among dengue patients admitted in Khon Kaen Hospital during June 2, 2007 to November 2, 2007. The objective of the study was to assess factors associated with shock among dengue patients admitted to Khon Kaen Hospital such as history, clinical manifestation and socio-demographic factors. This study was a hospital-based case-control study by using one part of history and clinical data before admission in hospital, which were taken from interviewing caregivers or patients and the other part of clinical data during admission in hospital, which were retrieved from hospital medical records.

#### 5.1 Statement of the Principal Findings

**The demographic and socio-economic characteristics of dengue patients and caregivers such as age, sex, nutrition status, education, residency, household's income and household's expenditure that had associations with DSS in Khon Kaen Hospital**

The present study found that age specific group < 10 years and studying in primary school had risk of developing DSS in crude analysis. It might be possible to explain that a half of DSS group was in children (age < 10 years = 54.1%) who were studying in primary school. The school was the place where children were together. Those who already had dengue virus and viraemia might transfer the disease to other children when getting bit by *Aedes aegypti* and *Aedes albopictus* mosquitoes at school. These relations had been supported by the annual report in Khon Kaen Hospital, which found that the majority number of DSS cases in Khon Kaen Hospital was in age group under 15 years old who admitted in pediatric ward in 2002 - 2005 (22). Likewise, DSS in Thailand and Khon Kaen province was highest in the age group 5-9 years old (15-19, 21).

Dengue shock syndrome tended to affect children under 10 years old (76). Many studies found that DSS was highest in the age specific group 5-9 years (33, 44) and many studies found that the DSS would increase in the age of 10-14 years old (20, 46, 50).

From the results of this study it was found that sex ratio (male: female) of dengue patients with DSS was 1.31:1 and male had higher risk to develop DSS when compared with female. This had been supported by reported dengue cases, who admitted in Khon Kaen Hospital, which found the proportion was higher in male than in female (22). Some epidemiologic studies suggested proportionately more males than female in DSS (36) like the study in Maldives in the 1999, which reported that it was surprising that for both the DF and DHF infections males suffered 2.7 times and 2.3 times more than females respectively (34). But some researches suggest that female had more risk to have DSS than male (28, 29). And many researches found that sex was no difference in risk to develop DSS (7, 8, 41). So it was not clear whether sex of patients was related to DSS.

The nutritional status of patients in age group 0-18 years and BMI of patients in age group  $\geq 18$  years old had no statistically significance association with in DSS in this study. It was found that data of height of many patients was not available in medical records, patients might reject to measure their heights because illness or health personnel was too busy, so nutritional status could not be calculated. But anyhow, the studies of Taweewong Tantracheewathorn and S. Tantracheewathorn found that the nutrition status was not statistically significant risk factor (61). Many previous studies found that DSS usually in patients who had good nutrition status (62) or obesity (26).

The dengue patients who were living in rural areas had higher risk to develop DSS than those who were living in urban areas in crude and multivariate analysis. It was mainly because most of the dengue patients with DDS (97.3%) lived in rural areas, which were in the epidemic zones. The other reason was that the general terrains of some districts in the rural areas in Khon Kaen province were mountains and forest, which were difficult to eradicate the breeding grounds of the mosquitoes. That was why there were many dengue patients who were in severe conditions and referred from other rural hospitals to Khon Kaen Hospital.

Caregivers who had household's income less than 6,000 baht/month or caregivers who had the household's expenditure more than 5,000 baht/month were found to be significant risk factors with DSS. Several possible reasons for explanation which

may be due to household's income and household's expenditure were important economic conditions of family for caregivers to take into consideration when they had to select choices of treatment for family member when they got sick (42). Among DSS group, mean household's expenditure was nearly the same as mean of household's income (6,352.6 baht and 5,125.3 baht respectively), which meant saving money was not possible. Loan from other for the payment of care or treatment could be found among dengue patients. But research from a case-control study in Fevela in Fortaleza during an outbreak of dengue fever found none of the socio-economic variable (family income) was a significant predictor for the occurrence of dengue fever (69).

**Clinical characteristics of patients before admission such as duration of fever before admission, underlying disease, muscle or joint pain, bleeding and abdominal pain that had associations with DSS in Khon Kaen Hospital**

This part of data was collected by interviewing dengue patients and caregivers. The average of duration of having fever before admitted in Khon Kaen Hospital in DSS group and non DSS group was  $4.7 \pm 1.1$  days and  $3.8 \pm 1.5$  days, respectively with statistically significant difference of means ( $p$ -value  $< 0.001$ ). The result agreed with the study in the six hundred and fifty DHF/DSS cases hospitalized during 1994- 1995. The mean number of fever days before hospitalization was 3.7 days for DHF cases and 4.2 days for DSS cases ( $p = 0.005$ ) (50). While mean of length of illness of dengue patients prior to admission was nearly longer such as the study in Venezuela found (mean 4.35 days vs. 3.26 days:  $p < 0.05$ ) (37). In North Queensland, Australia, it was found that mean duration symptoms of dengue patient prior to admission was 5 days (52). In the study in Chon Buri Regional Hospital, Thailand, it was found that patients with DHF had mean duration of having fever was 4.5 days before coming to the hospital (70) and the retrospective review in Children's Hospital (Inpatient Department - IPD) found that the duration of fever in DHF is 5.0 days and DSS was 4.8 days (8).

In this study, the dengue patients who had duration of fever before hospitalization within 5-8 days had higher risk to develop DSS. It could be the majority of DSS was referred cases and these cases had long duration of fever and this had been supported from WHO, 1997, which found that after 2-7 days of fever, a rapid fall in temperature was often accompanied by signs of circulatory disturbance of varying

severity (28). Since the duration of fever was related to DSS, at the end of the febrile phase (critical stage) public health authorities should monitor patients carefully. Some cases of dengue patients, DSS happened on 3<sup>rd</sup> of symptom (had fever 2 days) or 8<sup>th</sup> of symptom (had fever 7 days) (2), so the duration of fever before hospitalization was important information for public health authorities for careful monitoring and proper managing in preventive intervention of Dengue Shock Syndrome.

The results of this study showed Diabetes mellitus, Hypertension, Renal insufficiency, Thalassemia, G-6-PD deficiency with no statistically significance risks. This result was not agreed with the study of Min-Sheng Lee, et al., which found that the multiple logistic regression analysis revealed a significant association between DHF/DSS with Diabetes mellitus, Hypertension and Renal insufficiency (51). It was because most of dengue patients in this study had no underlying disease.

History of the illness with dengue before in dengue patients was not significant risk to develop DSS as in many studies confirmed that the secondary infection in dengue patients was related to DSS (9, 29, 36, 51, 54, 56, 61). It could be possible reason in recalled error from interviewing that the dengue patients or caregivers forgot or did not know that the patients had history of dengue illness before.

From interviewing and crude analysis, it was found that the dengue patients who did not have muscle or joint pain had higher risk to develop DSS. The muscle or joint pain was common symptoms in dengue patient (3-6). In this study, it was found that patients with DSS had muscle or joint less than in non DSS group (56.8 % and 77.5% respectively). Thus, in the group of patients without muscle and joint pain, it was the protective factor in developing DSS. However, further study was highly recommended for this point of view if recalled error in this study was rare.

Bleeding before hospitalization had high risk in developing DSS. This result agreed with the study in Children in BMA Medical College and Vajira Hospital which found that bleeding was risk factor of DSS (adjusted OR = 5.1, 95%CI : (1.5 - 17.1) (61). The explanation was that since definition of bleeding before admission in this study referred to many signs of bleeding such as small red spots on the skin, spontaneous bruises, nose bleeding, gum bleeding and bleeding in other sites. One among other criteria for admission of referred cases in Khon Kaen Hospital was patients, who had signs of bleeding. 94.6% of DSS patients in this study were referred cases and 33.0% of total

study population had bleeding sign. Probably, knowledge in DF, DHF and DSS among this group of patients was good, when they had bleeding they preferred to come to this hospital. From pathophysiological point of view, it could be explained that the bleeding diathesis was caused by vaculopathy, thrombocytopenia, platelet dysfunction and caugolopathy (77, 78). Massive bleeding that required blood transfusion was less common and usually occurred after the onset of shock (2, 3, 6, 27, 28). The present study found that bleeding in the early course of the disease before defervescence, including epistaxis, bleeding per gum, hematemesis and melena was one of the risks of shock. Bleeding in the early course of the disease should alarm the clinicians that the dengue patients were at risk of shock.

Abdominal pain produced risk to DSS in this study. Abdominal pain found in severe cases of dengue, and was obvious and sometime unbearable symptom. And majority of participants in this study had abdominal pain. These groups of patients were usually and immediately admitted in Khon Kaen Hospital with closed supervision for treatment and care. This finding had been supported by National Guideline for Clinical Management of Dengue Syndrome, which suggested that abdominal pain was a dangerous signs for close observation. The dengue patients should be taken to the hospital, because these signs were the early stage of shock (4). Acute abdominal pain was a frequent complaint shortly before the onset of shock (28, 78).

#### **Clinical characteristics of dengue patients during admission considered to be significantly associated with development of DSS in Khon Kaen Hospital**

Hemorrhagic manifestations of dengue patients such as, gum bleeding and hematemesis or melena and epigastric pain was found in severe cases and usually significantly associated with DSS. This was because patients with DHF grades II, III and IV always had spontaneous bleeding. These group of studied patients had such bleeding sign, so they had to be admitted in hospital as soon as possible (2, 78). Massive bleeding that required blood transfusion was less common and usually occurred after the onset of shock (2, 3, 6, 27, 28). Bleeding in the early course of the disease should alarm the clinicians that the dengue patients were at risk of shock. This relationship had been supported from study in Children in BMA Medical College and Vajira Hospital found that bleeding was risk factor of DSS (61).

This study showed the association between of negative tourniquet test and DSS. It might be that this factor was retrieving from medical records and sometimes error in recording occurred because many staffs had different skill. This study might have some measurement error from non skill health personnel which could produce false positive. Having prolonged fever and long period of time before admission also affected the result of tourniquet test. (The average of duration of fever before admitted in Khon Kaen Hospital in DSS group and non DSS group was  $4.7 \pm 1.1$  days and  $3.8 \pm 1.5$  days, respectively). This finding was supported by the result of tourniquet test, which yielded the false positive result. That meant that the dengue patients had fever several days prior to receiving the tourniquet test (4, 79). This result had been supported by the study in risk factors of dengue shock syndrome in children, which found that having positive of tourniquet test had no statistical difference between DHF and DSS groups (61). But anyhow, there were many researches suggested the determined risk factor of DSS was positive tourniquet test (29, 72).

The results from this study showed that the dengue patients who had epigastric/abdominal pain during admission in hospital had higher risk to develop DSS when compared to those who did not have epigastric/abdominal pain with statistical significance in crude analysis. That should be explained by some dengue patients admitted in Khon Kaen Hospital, who usually had severe signs such as bleeding or abdominal pain these sign was criteria for admission with dengue patients. Referred cases from another hospital usually had severe sign specially had abdominal pain, caregivers concern about survival of dengue patients and felt more confident in doctors, equipment in Khon Kaen Hospital including public health staff. Thus, most of the caregivers requested to refer their dengue patients to Khon Kaen Hospital. This had been supported by National Guideline for Clinical Management of Dengue Syndrome, which suggested that all dengue patients must be carefully observed for complications, patients and households should be informed that severe abdominal pain was one of the dangerous signs. If this sign was noticed, the patients should be taken into the hospital because these signs were in the early stage of shock (4) and acute abdominal pain was a frequent complaint shortly before the onset of shock (28).

*Symptoms of plasma leak and results from laboratory test and referred case*

In this study, dengue patients who had symptoms of plasma leak (pleural effusion and ascites) or platelet less than 100,000 cells/mm<sup>3</sup> or WBC less than 5,000 cells/mm<sup>3</sup> had higher risk to develop DSS. This should be explained that some DSS cases were referred cases or cases with severe signs and symptom from another hospital (rural area). These signs were found before and during admission in Khon Kaen Hospital such as plasma leak (pleural effusion and ascites) or platelet less than 100,000 cells/mm<sup>3</sup> or WBC less than 5,000 cells/mm<sup>3</sup>. This finding had been supported by the pathophysiology of DSS leading to a fatal outcome that increased vascular permeability, plasma leakage including hemoconcentration, hypoproteinemia /hypoalbuminemia, pleural effusion, ascites, threatened shock and profound shock and coagulopathy including thrombocytopenia leading to disseminated intravascular coagulation and massive hemorrhage (77, 80). The evidence of many researches found that DHF with plasma leakage that might lead to hypovolumic shock, dengue shock syndrome (DSS) (2, 3, 7) and these symptoms (ascites and pleural effusion) were the signs of plasma leakage (23, 28) so these factors were related to DSS too. The pleural effusion had been supported by the study of Venezuela found that vascular leakage was also associated with illness severity of DHF on admission (OR = 14.3,  $p < 0.005$ ) (37) and it was positively correlated with disease severity (3).

Having the platelet less than 100,000 cells/mm<sup>3</sup> related to DSS. This had supported that thrombocytopenia and hemoconcentration always occurred together. Decreasing of platelet occurred before hemoconcentration. Both signs occurred before decreasing of fever and shock (78). The results had been supported by the platelet counts usually decreased significantly in all groups of dengue with high severity ( $p$ -value  $< 0.001$ ) (9) and thrombocytopenia less than 100,000 cells/mm<sup>3</sup> (29, 73) or the low platelet count less than 50,000 cells/mm<sup>3</sup> related to shock with dengue (61, 72).

White blood cell had higher risk to develop dengue with shock. It could be explained that in DHF, the white blood cell count might be variable at the onset of illness, ranging from leucopenia to mild leukocytosis, but a drop in the total white blood cell count due to a reduction in the number of neutrophils was virtually always observed near the end of the febrile phase of illness. Relative lymphocytosis, with the presence of atypical lymphocytes, was a common finding before defervescence or shock (28, 78). The

relationship had been supported by the study in risk factors of dengue shock syndrome in children which found that WBC less than 5,000 cells/mm<sup>3</sup> associated with DSS by univariate analysis (61).

Dengue patients who had abdominal distension had significantly higher risk to develop DSS in crude analysis. This finding could be explained that the majority of the participants with DHF and DSS in this study had plasma leak and related to abdominal distension. This finding had been supported by WHO, 1997, which suggested that epigastric discomfort and tenderness at the right costal margin were common in DHF patients (28).

Enlargement of liver had significantly higher risk to develop DSS in the crude and multivariate analysis. It was because DSS cases in this study were severe cases and including referred cases from other hospitals from epidemic area. These patients had a symptoms or fever for long period of time before admission in Khon Kaen Hospital. Some DSS cases had repeated shock during admission in Khon Kaen Hospital. This finding had been supported by many previous studies, which found that the determined risk factors of DSS found in enlargement of liver (29). The liver organ was usually palpable in early in the febrile phase and varied in size from just palpable to 2-4 cm. at below the costal margin. Although liver size was not correlated with disease severity, an enlarged liver was observed more frequency in shock than in non-shock cases (3, 81).

Some interesting factor that should be mentioned even it was not included in the model of multivariate but in crude analysis which was being referred cases. Referred cases were significant risk for DSS. It could be because Khon Kaen Hospital was the regional hospital. Health service provided for the population in Khon Kaen province and population of other provinces nearby were at every level of care: primary, secondary and tertiary care so when dengue patients had more severe signs, these patients was referred to Khon Kaen Hospital. Caregivers were concerned about survival of dengue patients and felt more confident in doctors, equipment in Khon Kaen Hospital including public health staffs. Thus, most of caregivers requested to refer dengue patients to Khon Kaen Hospital. This relation had been supported by Guideline for treatment and diagnosis of dengue hemorrhagic fever in Thailand, which suggested that referred cases were at risk for DSS(2).

### *Symptoms of hypoperfusion*

The result demonstrated risk to develop DSS among patients who had lethargy and restlessness which were related to DSS in crude analysis. These results had been supported from many researches, who found that lethargy and restlessness were commonly found in DSS (4, 10, 23, 28). Common signs of complication observed during the a febrile phase of DHF Grade III usually included circulatory failure manifested by rapid and weak and narrowing of the pulse pressure and hypotension, characterized by high diastolic pressure relative to systolic pressure (e.g. 90/80) and the presence of cold clammy skin and restlessness. Immediately after hospitalization the hematocrit, platelet count and the vital signs should be examined to assess condition of the patient, and intravenous fluid therapy should be started (4).

## **5.2 Strength and Weaknesses of the Study**

### **5.2.1 Strength of the Study**

The place or site of this study was a regional hospital with services care on all levels of health care: primary, secondary and tertiary care. The validity and the usefulness of result of study would be fully achieved and could be used for generalizability to those regional hospitals as well as district hospitals.

### **5.2.2 Weaknesses of the Study**

1. Some clinical data from laboratory, such as Hematocrit, WBC and platelet counts of the study population referred from other hospitals before admitted in hospital were not traced due to time, budget and availability of permission.
2. This study was based mainly on clinical information because of limitation of budget and did not have laboratory diagnosis of dengue infection and type of dengue using PCR nor the diagnosis of dengue infection using ELISA.

## **CHAPTER 6**

### **CONCLUSION AND RECOMMENDATION**

The present study was a hospital-based case-control study which had been conducted among 215 patients admitted with dengue from 2<sup>nd</sup> June 2007 to 2<sup>nd</sup> November 2007 in Khon Kaen Hospital, Thailand. The study was aimed to find factors related to the state of having shock among dengue patients.

The sex ratio (male : female) was found to be higher in male than female among DSS group and nearly equal proportion among non DSS group. The mean (SD) ages of DSS group was significantly higher than those of non DSS group. Nearly all of DSS patients and about fourthly percent of non DSS group lived in rural areas. Most of DSS patients and one-third of non DSS group were referred cases. More than half of caregivers of the patients were their mothers with the mean (SD) age of 42 (10) years and most of them finished primary school. Two-fifths and one-fifth of caregivers of patients in DSS group and non DSS group had the occupation in agriculture. Three-fourths of caregivers had the average household's income and household's expenditure in DSS group at less than 6,000 Baht and more than 5,000 Baht, respectively.

Most of the patients in DSS group had duration of fever 0-4 days before admitted in Khon Kaen Hospital. Most of the patients in both groups had no underlying diseases.

Before admission in Khon Kaen Hospital, three-quarters of the patients in DSS group were reported of having vomiting, dizziness and headache. More than half of the patients in DSS group were reported that they had reduction of urine output, muscle or joint pain, bleeding and diarrhea. Most of the patients in non DSS group were reported of having dizziness, headache and muscle or joint pain. About two-thirds of these patients had vomiting and a half of this group had epigastric/abdominal pain and diarrhea.

The clinical manifestations of the patients during admitted in Khon Kaen Hospital from medical records, it was found that most of the patients in DSS group had

anorexia and epigastric pain, more than half had rash and a half had headache and vomiting.

Most of the patients in DSS group and non DSS group had experience of any hemorrhagic manifestations. More than half of the patients in DSS group had positive tourniquet test and hematemesis or melena. One-fourth had petechiae. One-third of these groups of patients had epistaxis and gum bleeding. A quarter of non DSS group of patients had hematemesis or melena.

All patients in DSS group had clinical evidence of plasma leak. Half of the patients in DSS group had pleural effusion and abdominal pain. Two-fifths of this group had ascites and enlargement of liver. One-third and two-fifths of non DSS group had abdominal pain and enlargement of liver.

Symptoms of hypoperfusion in dengue patients found in most of patients in DSS group included narrow pulse pressure or small volume pulse volume, cold extremities, lethargy and restlessness. Two-thirds and three-fourths of these patients had slow capillary refill or clammy skin and oliguria. Most of these patients had final interpreted of platelet counts lower than  $100,000 \text{ cells/mm}^3$ . Most of the patients in non DSS group had white blood cell lower than  $5,000 \text{ cells/mm}^3$  and more than half of this group had lethargy or final interpreted of platelet counts lower than  $100,000 \text{ cells/mm}^3$ .

In the univariate analysis, the factors found to be significantly associated with severity of DHF were demographic variables: age of patients, socio-economic variables: education (studying) of patients, residency, household's income and expenditure, symptoms of patients before admission in hospital: duration of fever before admitted in hospital, having muscle or joint pain, having bleeding and having abdominal pain, clinical characteristics of patients during admission in hospital: signs and symptoms, epigastric pain, gum bleeding, hematemesis, symptoms of plasma leak: pleural effusion, abdominal distension, enlargement of liver and ascites, symptoms of hypoperfusion: lethargy and restlessness results from laboratory test and referred case: platelet counts, white blood cell and being referred case.

It was well recommended that sex was the only risk indicator or risk marker which was an attribute that was associated with an increased probability of occurrence of DSS which was not necessarily a causal factor. The result from multivariate analysis found that male had higher risk to develop DSS when compared with female. Careful

monitory in dengue hemorrhagic fever patients to prevent DSS should be among male more than female among this group of study population.

Living in the rural area was risk to DSS. In Thailand, rural areas usually were the risk areas for disease transmission, because there were many breeding places of mosquito such as big water containers and big jar.

### **Recommendations from the Finding of the Study**

1. The results from the study were useful to help health personnel to know about characteristics of dengue patients who might have risks to shock and would add the knowledge on pathophysiology of DSS for those who would consider proper management and preventive intervention of DSS.

2. Although signs and symptoms of having no muscle or joint pain before admission, having bleeding before admission in the hospital, negative tourniquet test, enlargement of liver during admission in the hospital and having ascites during admission in the hospital were significant factors that were not preventable, these signs and symptoms would be used to develop useful guidelines for monitoring patients with dengue who would be at risk of having shock. Also, the progression of DSS could be prevented by close monitoring for early signs of shock, and prompt and adequate replacement of plasma leakage must be performed to prevent death.

3. Health education to prevent dengue fever, i.e. improving knowledge of dengue disease in children, caregivers and people, should be emphasized in rural areas. Activities of local health personnel should be emphasized on detection for Breteau Index (BI) and House Index (HI) (for residential households) and container index (CI) (for nonresidential places) in order to prevent rural area from dengue.

4. During admission in hospital in the early course of the disease should be alarming for significant signs and symptoms for clinicians that the dengue patients were at risk of shock. Prompt and adequate fluid replacement could be given on time to prevent the progression of shock.

## **Recommendations for Further Studies**

1. Place or site of further studies should be in the areas having high incidence of dengue to have sufficient number of cases for the analyses.

2. Results from further studies conducted in district hospitals which locate quite far from regional hospitals would be useful to apply the results to district level.

3. In the further studies, the clinical data should be completely collected prior to admission such as laboratory data, Hematocrit, WBC and platelet counts to find the factors related to DSS.

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## **APPENDIX**

## **APPENDIX A**

### **Questionnaire**

#### **Title: Factors related to shock among dengue patients in Khon Kaen Hospital, Thailand**

#### **Dear, Dengue patient and dengue patient's caregiver**

This questionnaire was used to interview you (dengue patient and dengue patient's caregiver) such as age, gender, weight, height, education level, occupation, residency, household's income, household's expenditure and clinical data.

#### **This questionnaire covers all the questions device to 4 parts**

Part1 Dengue patient's factor (Interview dengue patient)

Part 2 Dengue patient's caregiver factors (Interview dengue patient's caregiver)

Part 3 The clinical data of dengue patient before admission in Khon Kaen Hospital (Interview dengue patient and/or dengue patient's caregiver)

Part 4 The clinical data of dengue patient during admission in Khon Kaen Hospital (Researcher retrieving data from medical record when Khon Kaen Hospital would allow)

Researcher confirms that, your answer will be in anonymous condition. There is no scope that any one can link your name with your answer on the questionnaire. Only the researcher will have an access to the questionnaire. After the data have been entered into a computer, the questionnaire will be destroyed. In case of publication, we will not include any sort of information that help you to identify.

Thank you for you kind and agreed to participant in this project.

Miss Siriyaporn Khuntason

Researcher

## Questionnaire

### For dengue patient (Part 1)

ID.....

Hospital number.....

Admission Date.....

1000 dengue patient			
Q 1001	Location of interview	1. Out patient 2. Emergency room 3. Pediatric ward 4. Pediatric intensive care unit 5. Medical ward	
Q 1002	Gender	1. Male 2. Female	
Q 1003	Age (years/month)	...../...../.	
Q 1004	Weight/Height	.....km./.....cm.	
Q 1005	What is the currently education?	1. Studying 2. Complete 3. No formal education	
* If no formal education, go to Q1006 If studying or complete go to Q1007			
Q 1006	What is the reason the patient no formal education	1. Never formal education 2. Young and not enough for entry school	
Q 1007	What is the patient's highest of education	1. Primary school 2. High school not complete 3. High school complete 4. Vocation school 5. College or more	
Q 1008	Residency	1. Urban 2. Rural	
Q 1009	Occupation	1. Government employee 2. Employee 3. Self-employed/merchant 4. Agriculture 5. Non-government employee 6. Not working for pay	
* If not working to pay go to Q1010 If choose choice 1,2,3,4,5 go to Q1011			
Q 1010	What is the reason the patient is not currently working for pay?	1. Student 2. House wife 3. Doing unpaid job 4. Retired/ too old 5. Looked but can't find 6. Ill health 7. Other.....	
Q 1011	Having history of illness with dengue before.	1. Yes 2. No	

.....  
Interviewer

.....  
Date of this interview

## Questionnaire

### For dengue patient's caregiver (Part 2)

ID.....

**Hospital number**.....

2000 Dengue patient's caregiver			
Q 2001	Relationship with dengue patients	1. Mother                      2. Father 3. Grandmother      4. Grandfather 5. Older, younger brother or sister of patients 6. Other.....	
Q 2002	Age of caregiver	..... years	
Q 2003	What is the currently education?	1. Studying    2. Complete 3. No formal education	
Q 2004	What is the patient's highest of education	1. Primary school 2. High school not complete 3. High school complete 4. Vocation school 5. College or more	
Q 2005	Occupation	1. Government employee    2. Employee 3. Self-employed/merchant 4. Agriculture 5. Non-government employee 6. Not working for pay	
* If not working to pay go to Q 2006    If choose choice 1,2,3,4,5 go to Q 2007			
Q 2006	What is the reason the patient is not currently working for pay?	1. Student                      2. House wife 3. Doing unpaid job    4. Retired/ too old 5. Looked but can't find 6. Ill health                      7. Other.....	
Q 2007	Household's income	.....Baht/Month	
Q 2008	Household's expenditure	.....Baht/Month	

.....  
Interviewer

.....  
Date of this interview

## Questionnaire

### For dengue patient and/or dengue patient's caregiver (Part 3)

ID.....

**Hospital number**.....

3000 Symptoms or signs of patient before admit in Khon Kaen Hospital
----------------------------------------------------------------------

Q 3001	Interviewee	1. Patient	2. Caregiver	3. Both
Q 3002	Number of fever before admission in Khon Kaen Hospital	.....(day)		

Did the patient have any of the following symptoms or signs before admission in Khon Kaen Hospital?

Q 3003	Vomiting	1. Yes	2. No	
Q 3004	Dizziness	1. Yes	2. No	
Q 3005	Excessive thirst	1. Yes	2. No	
Q 3006	Reduced urine output	1. Yes	2. No	
Q 3007	Headache	1. Yes	2. No	
Q 3008	Skin rash	1. Yes	2. No	
Q 3009	Eye pain	1. Yes	2. No	
Q 3010	Muscle or joint pain	1. Yes	2. No	
Q 3011	Bleeding (small red spots on the skin, spontaneous bruises, nose bleeding, gum bleeding other bleeding)	1. Yes	2. No	
Q 3012	Abdominal pain	1. Yes	2. No	
Q 3013	Diarrhea	1. Yes	2. No	
Q 3014	Sore throat	1. Yes	2. No	
Q 3015	Running nose	1. Yes	2. No	

.....  
Interviewer

.....  
Date of this interview

**Medical record (Part 4)**  
**(Retrieving by researcher)**

**Hospital number**.....

		ID	
qm 001	Admission Date (Date/month/year)		
qm 002	Diagnosis of admission	1. Non-dengue illness 2. Dengue Fever 3. Dengue Hemorrhagic Fever 4. Dengue Shock Syndrome	
qm 003	If diagnosis at admission dose not mention “dengue”, please report the diagnosis mentioned.	Specify.....	
qm 004	Discharge date (Date/month/year)	...../...../.....	
qm 005	Diagnosis at discharge	1. Non-dengue illness 2. Dengue Fever 3. Dengue Hemorrhagic Fever 4. Dengue Shock Syndrome	
qm 006	How many days did the patient have fever (body temperature more than 38.5 C) during admission?	.....days	
qm 007	Having history of illness with Diabetes mellitus	1. Yes    2. No	
qm 008	Having history of illness with Hypertension	1. Yes    2. No	
qm 009	Having history of illness with Renal insufficiency	1. Yes    2. No	
qm 010	Having history of illness with Thalassemia	1. Yes    2. No	
qm 011	Having history of illness with G – 6 – PD deficiency	1. Yes    2. No	

12 – 19 Did the patient have any of the following symptoms or signs during admission in Khon Kaen Hospital?			
qm 012	Headache	1. Yes    2. No	
qm 013	Retro-orbital pain	1. Yes    2. No	
qm 014	Myalgia/arthritis	1. Yes    2. No	
qm 015	Anorexia	1. Yes    2. No	
qm 016	Rash	1. Yes    2. No	
qm 017	Vomiting	1. Yes    2. No	
qm 018	Epigastric pain	1. Yes    2. No	
qm 019	Excessive thirst	1. Yes    2. No	

20 – 28 Did the patient have any of the following Hemorrhagic manifestations during admission in Khon Kaen Hospital?			
qm 020	Hemorrhagic manifestations	1. Yes	2. No
qm 021	Positive tourniquete test	1. Yes	2. No
qm 022	Petechiae	1. Yes	2. No
qm 023	Purpura	1. Yes	2. No
qm 024	Echymosis? (a small haemorrhagic spot, larger than a petechia, in the skin or mucous membrane)	1. Yes	2. No
qm 025	Epistaxis	1. Yes	2. No
qm 026	Gum bleeding	1. Yes	2. No
qm 027	Hematemesis/Melena	1. Yes	2. No
qm028	Other bleeding? Specify	.....	

29 – 33 Did the patient have any of the following symptoms or signs of plasma leak during admission in Khon Kaen Hospital?			
qm029	Leak of plasma	1. Yes	2. No
qm030	Pleural effusion	1. Yes	2. No
qm031	Abdominal distension	1. Yes	2. No
qm032	Enlargement of liver	1. Yes	2. No
qm033	Ascites	1. Yes	2. No

34 – 43 Did the patient have any of the following symptoms or signs of DSS during admission in Khon Kaen Hospital?			
qm034	Hypoperfusion	1. Yes	2. No
qm 035	Narrow pulse pressure or small pulse volume	1. Yes	2. No
qm 036	Cold extremities	1. Yes	2. No
qm 037	Slow capillary refill	1. Yes	2. No
qm 038	Clammy skin	1. Yes	2. No
qm 039	Lethargy	1. Yes	2. No
qm 040	Restlessness	1. Yes	2. No
qm 041	Oliguria	1. Yes	2. No
qm 042	Report the <u>lowest systolic</u> blood pressure written in the record	Specify.....	
qm 043	Report the <u>concurrent diastolic</u> blood pressure written in the record at the time of the lowest systolic blood pressure	Specify.....	

44 – 46 Other clinical manifestation of patient during admission in Khon Kaen Hospital.			
qm 044	Clinical manifestation 1		
qm 045	Clinical manifestation 2		
qm 046	Clinical manifestation 3		

47 – 54 Results of Laboratory testes of dengue patients during admission in Khon Kaen Hospital			
qm 047	Report the lowest hematocrit value at first day's admission in Khon Kaen Hospital (If patient had hematocrit test)	.....%	
qm 048	Report the highest hematocrit before any intravenous fluid therapy	.....%	
qm 049	Report the lowest hematocrit value during the hospitalization	.....%	
qm 050	Increasing hematocrit	1. $\geq 20\%$ 2. $< 20\%$	
qm 051	Report the lowest platelets count	.....per mm <sup>3</sup>	
qm 052	Report the highest platelets count	.....per mm <sup>3</sup>	
qm 053	Report the highest white blood cell count	.....per mm <sup>3</sup>	
qm 054	Report the lowest white blood cell count	.....per mm <sup>3</sup>	

55 – 60 Results of Laboratory testes of dengue patients during admission in Khon Kaen Hospital			
qm 055	Did the patient receive any thoracic X-RAY?	1. Yes    2. No	
qm 056	If yes, was there any evidence of pleural/pericardium effusion	1. Yes    2. No	
qm 057	Did the patient receive any ultrasonograms?	1. Yes    2. No	
qm 058	If yes, was there any evidence of pleural/pericardium effusion	1. Yes    2. No	
qm 059	Was there evidence of liver enlargement or ascites?	1. Yes    2. No	
qm 060	Did the patient receive any serotype test? If yes, Please specify.....	1. Yes    2. No	

.....  
Interviewer

.....  
Date of this interview

## APPENDIX B

### โครงการ การศึกษาปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออก ในโรงพยาบาลขอนแก่น ประเทศไทย แบบเก็บข้อมูล

#### เรียนผู้ป่วยไข้เลือดออกและญาติผู้ดูแลผู้ป่วยไข้เลือดออก

แบบเก็บข้อมูลนี้ประกอบด้วยแบบสอบถามที่จะสอบถามเกี่ยวกับตัวท่าน(ผู้ป่วยไข้เลือดออกและญาติผู้ดูแลผู้ป่วยไข้เลือดออก) ได้แก่ อายุ เพศ น้ำหนัก ส่วนสูง ระดับการศึกษา อาชีพ ที่อยู่ รวมถึงรายได้ ในครัวเรือน และลักษณะอาการป่วยต่าง ๆ ของผู้ป่วยไข้เลือดออก

#### ข้อมูลมีทั้งหมด 4 ส่วน โดยมีรายละเอียดดังต่อไปนี้

ส่วนที่ 1 รายละเอียดของผู้ป่วย (สัมภาษณ์ผู้ป่วยไข้เลือดออก)

ส่วนที่ 2 รายละเอียดของผู้ดูแลผู้ป่วยอย่างใกล้ชิดก่อนที่มารับการรักษาพยาบาลเป็นผู้ป่วยในของโรงพยาบาลขอนแก่น (สัมภาษณ์ญาติผู้ดูแลผู้ป่วยไข้เลือดออก)

ส่วนที่ 3 อาการของผู้ป่วยตั้งแต่เริ่มมีไข้ก่อนที่จะมารับการรักษาที่โรงพยาบาลขอนแก่น (สัมภาษณ์ผู้ป่วยและ/หรือญาติผู้ดูแลผู้ป่วย)

ส่วนที่ 4 ข้อมูลการอาการเจ็บป่วยด้วยไข้เลือดออกของผู้ป่วยระหว่างที่มารับการรักษาเป็นผู้ป่วยในของโรงพยาบาลขอนแก่น (ผู้วิจัยขอคัดลอกจากเวชระเบียนเมื่อได้รับอนุญาตจากทางโรงพยาบาล)

ผู้วิจัยขอรับรองว่าคำตอบที่ได้จากท่าน (ผู้ป่วยไข้เลือดออกและญาติผู้ดูแลผู้ป่วยไข้เลือดออก) จะถูกเก็บเป็นความลับไม่ถูกนำมาเปิดเผยในชื่อของท่าน โดยผู้วิจัยจะนำมาใช้ในภาพรวมและแบบเก็บข้อมูลจะถูกทำลายทันทีหลังจากการทำวิจัยเสร็จสิ้นแล้ว

ขอขอบพระคุณเป็นอย่างสูงที่ท่านสละเวลาในการตอบแบบเก็บข้อมูลฉบับนี้

นางสาวศิริญาพร ชันทะสอน

ผู้วิจัย

**แบบสัมภาษณ์ผู้ป่วย (ส่วนที่ 1)**

เลขที่แบบสัมภาษณ์.....

หมายเลขบัตรโรงพยาบาล.....

วันที่รับเป็นคนไข้ใน.....

1000 รายละเอียดผู้ป่วย			
Q 1001	สถานที่ที่ทำการสัมภาษณ์	1. ตึกผู้ป่วยนอก 2. ห้องฉุกเฉิน 3. ตึกเด็กโต 4. PICU 5. อายุรกรรม	
Q 1002	เพศ	1. เพศชาย 2. เพศหญิง	
Q 1003	อายุ (ปี/เดือน)	...../...../.....	
Q 1004	น้ำหนัก/ส่วนสูง	.....กก./.....ซม.	
Q 1005	ท่านกำลังเรียนอยู่หรือไม่	1. กำลังเรียนอยู่ 2. จบแล้ว 3. ไม่ได้เรียน	
* ถ้าเลือกข้อไม่ได้เรียน ให้ตอบเหตุผลในข้อ Q1006 ถ้าเลือกข้อกำลังเรียนอยู่ หรือ จบแล้ว ให้ข้ามไปตอบข้อ Q1007			
Q 1006	เหตุผลที่ไม่ได้เรียน	1. ไม่ได้เรียนหนังสือเลย 2. ยังไม่ถึงเกณฑ์เข้าโรงเรียน	
Q 1007	การศึกษาของผู้ป่วย	1. ประถมศึกษา 2. มัธยมศึกษาตอนต้น 3. มัธยมศึกษาตอนปลาย 4. ปวช/ปวส 5.ปริญญาตรีหรือสูงกว่า	
Q 1008	ที่อยู่ปัจจุบันก่อนเข้ารับการรักษา	1. ในเมือง 2. ในชนบท	
Q 1009	อาชีพหลักของผู้ป่วยในปัจจุบัน	1. ลูกจ้างรัฐ/ข้าราชการ 2. รับจ้างทั่วไป 3. กิจการส่วนตัว/ค้าขาย 4. เกษตรกรรม 5. ลูกจ้างบริษัทเอกชน 6. ไม่ได้ประกอบอาชีพ	
* ถ้าไม่ได้ประกอบอาชีพให้ตอบข้อ Q1010		ถ้าประกอบอาชีพให้ข้ามไปตอบข้อ Q1011	
Q 1010	เหตุผลที่ไม่ได้ประกอบอาชีพ	1. กำลังเรียน 2. แม่บ้าน 3. ทำงานที่ไม่ได้จ่ายเป็นเงิน 4. อายุมาก/ชรา 5. ยังหางานไม่ได้ 6. สุขภาพไม่ดี 7. อื่นๆ โปรดระบุ.....	
Q 1011	ผู้ป่วยเคยป่วยเป็นไข้เลือดออกมาก่อนหรือไม่	1. เคย 2. ไม่เคย	

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ผู้สัมภาษณ์

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วันที่สัมภาษณ์

## แบบสัมภาษณ์ญาติผู้ป่วย (ส่วนที่ 2)

เลขที่แบบสัมภาษณ์.....

หมายเลขบัตรโรงพยาบาลของผู้ป่วย.....

2000 รายละเอียดของผู้ดูแลผู้ป่วย

Q 2001	ความสัมพันธ์กับผู้ป่วย	1. มารดา 2. บิดา 3. ตา-ยาย 4. ปู่-ย่า 5. พี่ชาย พี่สาว 6. อื่น ๆ โปรดระบุ	
Q 2002	อายุของผู้ดูแลผู้ป่วย (ปี)	..... ปี	
Q 2003	ท่านกำลังเรียนอยู่หรือไม่	1. กำลังเรียนอยู่ 2. จบแล้ว 3. ไม่ได้เรียนหนังสือ	
Q 2004	การศึกษา	1. ประถมศึกษา 2. มัธยมศึกษาตอนต้น 3. มัธยมศึกษาตอนปลาย 4. ปวช/ปวส 5.ปริญญาตรีหรือสูงกว่า	
Q 2005	อาชีพหลักของผู้ดูแลผู้ป่วยในปัจจุบัน	1. ลูกจ้างรัฐ/ข้าราชการ 2. รับจ้างทั่วไป 3. กิจการส่วนตัว/ค้าขาย 4. เกษตรกรรม 5. ลูกจ้างบริษัทเอกชน 6. ไม่ได้ประกอบอาชีพ	
* ถ้าไม่ได้ประกอบอาชีพให้ตอบข้อ Q 2006 ถ้าประกอบอาชีพให้ข้ามไปตอบข้อ Q 2007			
Q 2006	เหตุผลที่ไม่ได้ประกอบอาชีพ	1. กำลังเรียน 2. แม่บ้าน 3. ทำงานที่ไม่ได้จ่ายเงิน 4. อายุมาก/ชรา 5. ยังหางานไม่ได้ 6. สุขภาพไม่ดี 7. อื่นๆ โปรดระบุ.....	
Q 2007	รายได้ของครัวเรือนต่อเดือน	.....บาท/เดือน	
Q 2008	รายจ่ายของครัวเรือนต่อเดือน	.....บาท/เดือน	

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ผู้สัมภาษณ์.....  
วันที่สัมภาษณ์

แบบสัมภาษณ์ผู้ป่วย และ/หรือญาติผู้ป่วย (ส่วนที่ 3)

เลขที่แบบสัมภาษณ์.....

หมายเลขบัตรโรงพยาบาลของผู้ป่วย.....

3000 ข้อมูลการเจ็บป่วยของผู้ป่วยในครอบครัวนี้

Q 3001	ผู้ให้ข้อมูล	1. ผู้ป่วย	2. ญาติ	3. ทั้งญาติและผู้ป่วย
Q 3002	จำนวนวันของการมีไข้ก่อนเข้ารับการรักษา ในโรงพยาบาล	ระบุ.....(วัน)		

ผู้ป่วยมีอาการดังต่อไปนี้หรือไม่ ตั้งแต่เริ่มมีไข้ที่บ้านก่อนที่จะมารับการรักษาที่โรงพยาบาล

Q 3003	อาเจียน	1. มี	2. ไม่มี	
Q 3004	เวียนศีรษะ ตาลาย	1. มี	2. ไม่มี	
Q 3005	กระหายน้ำอย่างมาก	1. มี	2. ไม่มี	
Q 3006	ปัสสาวะน้อยครั้ง	1. มี	2. ไม่มี	
Q 3007	ปวดศีรษะ	1. มี	2. ไม่มี	
Q 3008	มีผื่นตามผิวหนัง	1. มี	2. ไม่มี	
Q 3009	ปวดตา	1. มี	2. ไม่มี	
Q 3010	ปวดกล้ามเนื้อหรือปวดตามข้อ	1. มี	2. ไม่มี	
Q 3011	มีเลือดออก(มีจุดเลือดเล็ก ๆ ตามผิวหนัง เลือดกำเดาไหล เลือดออกตามเหงือก)	1. มี	2. ไม่มี	
Q 3012	ปวดท้องน้อย	1. มี	2. ไม่มี	
Q 3013	ท้องร่วง	1. มี	2. ไม่มี	
Q 3014	เจ็บคอ	1. มี	2. ไม่มี	
Q 3015	มีน้ำมูก	1. มี	2. ไม่มี	

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ผู้สัมภาษณ์

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วันที่สัมภาษณ์

**แบบฉบับบันทึกข้อมูลจากเวชระเบียนผู้ป่วย (ส่วนที่ 4)**  
**(เก็บข้อมูลโดยผู้วิจัย)**

หมายเลขบัตรโรงพยาบาล.....

		รหัสผู้ป่วย ID	
qm 001	วันที่เข้ารับการรักษา (ระบุ ว/ด/ป)		
qm 002	การวินิจฉัยเมื่อแรกเข้ารับรักษา	1. Non-dengue illness 2. Dengue Fever 3. Dengue Hemorrhagic Fever 4. Dengue Shock Syndrome	
qm 003	การวินิจฉัยเป็นอย่างอื่น นอกเหนือจาก dengue	ระบุ.....	
qm 004	วันที่จำหน่าย (ระบุ ว/ด/ป)	...../...../.....	
qm 005	การวินิจฉัยวันที่จำหน่าย	1. Non-dengue illness 2. Dengue Fever 3. Dengue Hemorrhagic Fever 4. Dengue Shock Syndrome	
qm 006	จำนวนวันที่ผู้ป่วยมีอาการไข้ มากกว่า 38.5 C ในช่วงที่เข้ารับการรักษาในโรงพยาบาล	.....วัน	
qm 007	ผู้ป่วย มีประวัติป่วยเป็น Diabetes mellitus หรือไม่	1. ใช่ 2. ไม่ใช่	
qm 008	ผู้ป่วย มีประวัติป่วยเป็น Hypertension หรือไม่	1. ใช่ 2. ไม่ใช่	
qm 009	ผู้ป่วย มีประวัติป่วยเป็น Renal insufficiency หรือไม่	1. ใช่ 2. ไม่ใช่	
qm 010	ผู้ป่วย มีประวัติป่วยเป็น Thalassemia หรือไม่	1. ใช่ 2. ไม่ใช่	
qm 011	ผู้ป่วย มีประวัติป่วยเป็น G – 6 – PD deficiency หรือไม่	1. ใช่ 2. ไม่ใช่	

12 – 19 ผู้ป่วยมีอาการดังต่อไปนี้หรือไม่ ในช่วงที่เข้ารับการรักษาในโรงพยาบาลนอนแกล่น			
qm 012	ปวดหัว (Headache)	1. มี	2. ไม่มี
qm 013	ปวดตา (Retro-orbital pain)	1. มี	2. ไม่มี
qm 014	ปวดกล้ามเนื้อ ปวดข้อ (Myalgia/arthralgia)	1. มี	2. ไม่มี
qm 015	เบื่ออาหาร (Anorexia)	1. มี	2. ไม่มี
qm 016	มีผื่นแดงขึ้น (Rash)	1. มี	2. ไม่มี
qm 017	อาเจียน (Vomiting)	1. มี	2. ไม่มี
qm 018	ปวดท้อง/ปวดท้องน้อย (Epigastric pain)	1. มี	2. ไม่มี
qm 019	กระหายน้ำอย่างมาก (Excessive thirst)	1. มี	2. ไม่มี

20 – 28 ผู้ป่วยมีอาการดังต่อไปนี้หรือไม่ ในช่วงที่เข้ารับการรักษาในโรงพยาบาลนอนแกล่น			
qm 020	ผู้ป่วยเคยหรือมีอาการแสดงเกี่ยวกับการมีเลือดออก ( Hemorrhagic manifestations )	1. มี	2. ไม่มี
qm 021	ผลตรวจ tourniquete test เป็นบวก	1. มี	2. ไม่มี
qm 022	จุดแดงเล็กๆ (Petechiae) ที่ผิวหนัง	1. มี	2. ไม่มี
qm 023	Purpura	1. มี	2. ไม่มี
qm 024	Echymosis? ( จุดแดงเล็กๆ ใหญ่กว่า petechia)	1. มี	2. ไม่มี
qm 025	เลือดกำเดาไหล (Epistaxis)	1. มี	2. ไม่มี
qm 026	เลือดออกที่เหงือก (Gum bleeding )	1. มี	2. ไม่มี
qm 027	อาเจียนเป็นเลือด (Hematemesis) / ถ่ายอุจจาระมีสีดำมีเลือดปน (Melena )	1. มี	2. ไม่มี
qm028	มีเลือดออกบริเวณอื่นๆ อีกหรือไม่ ถ้ามีโปรดระบุ	ระบุ.....	.....

29 – 33 ผู้ป่วยมีอาการดังต่อไปนี้หรือไม่ ในช่วงที่เข้ารับการรักษาในโรงพยาบาลนอนแกล่น			
qm029	พลาสมารั่ว ( Leak of plasma)	1. มี	2. ไม่มี
qm030	น้ำท่วมปอด มีน้ำในปอด (Pleural effusion)	1. มี	2. ไม่มี
qm031	ท้องบวม (Abdominal distension)	1. มี	2. ไม่มี
qm032	ตับโต (Enlargement of liver)	1. มี	2. ไม่มี
qm033	น้ำในช่องท้อง (Ascites )	1. มี	2. ไม่มี

34 – 43 ผู้ป่วยมีอาการดังต่อไปนี้หรือไม่? ในช่วงที่เข้ารับการรักษาในโรงพยาบาลขอนแก่น			
qm034	ผู้ป่วยมีอาการ Hypoperfusion	1. มี	2. ไม่มี
qm 035	ผู้ป่วยมีอัตราการเต้นของหัวใจถี่/ความดันต่ำ หรือไม่ (Narrow pulse pressure or small pulse volume)	1. มี	2. ไม่มี
qm 036	ปลายมือ ปลายเท้าเย็น (Cold extremities)	1. มี	2. ไม่มี
qm 037	หลอดเลือดฝอย (Slow capillary relief)	1. มี	2. ไม่มี
qm 038	ผิวหนังชื้น-เย็น (Clammy skin)	1. มี	2. ไม่มี
qm 039	เซื่องซึม (Lethargy)	1. มี	2. ไม่มี
qm 040	หงุดหงิด กระวนกระวาย (Restlessness)	1. มี	2. ไม่มี
qm 041	ปัสสาวะน้อย (Oliguria)	1. มี	2. ไม่มี
qm 042	ค่าความดัน systolic ต่ำที่สุดที่ปรากฏในทะเบียนผู้ป่วย	ระบุ.....	
qm 043	ค่าความดัน diastolic ที่คู่กับค่าความดัน systolic ต่ำที่สุดที่ปรากฏในทะเบียนผู้ป่วย	ระบุ.....	

44 – 46 ลักษณะอาการทางคลินิกอื่น ๆ ในผู้ป่วยไข้เลือดออกในช่วงที่เข้ารับการรักษาในโรงพยาบาลขอนแก่น			
qm 044	Clinical manifestation 1 อาการแสดงทางคลินิก		
qm 045	Clinical manifestation 2 อาการแสดงทางคลินิก		
qm 046	Clinical manifestation 3 อาการแสดงทางคลินิก		

47 – 54 ผลตรวจทางห้องปฏิบัติการในช่วงที่เข้ารับการรักษาในโรงพยาบาลขอนแก่น			
qm 047	% Hct น้อยที่สุดในวันแรกที่ได้รับรักษาในรพ.ขอนแก่น (กรณีที่มีการเจาะเลือด)	.....%	
qm 048	% Hct มากที่สุดก่อนการให้สารน้ำทางหลอดเลือดดำ	.....%	
qm 049	% Hct น้อยที่สุดในช่วงที่เข้ารับการรักษาในโรงพยาบาล	.....%	
qm 050	การเพิ่มขึ้นของ Hct ของผู้ป่วย	1. $\geq 20\%$ 2. $< 20\%$	
qm 051	Platelets ต่ำสุด	.....per mm <sup>3</sup>	
qm 052	Platelets สูงสุด	.....per mm <sup>3</sup>	
qm 053	จำนวน White Blood Cell สูงสุด	.....per mm <sup>3</sup>	
qm 054	จำนวน White Blood Cell ต่ำสุด	.....per mm <sup>3</sup>	

55 – 60 ผลการตรวจในช่วงที่เข้ารับการรักษาในโรงพยาบาลขอนแก่น			
qm 055	ผู้ป่วยได้รับการตรวจ X-RAY หรือไม่	1. มี 2. ไม่มี	
qm 056	ถ้ามี ผู้ป่วยมีอาการน้ำท่วมปอด (pleural/pericardium effusion) หรือไม่	1. มี 2. ไม่มี	
qm 057	ผู้ป่วยได้รับการตรวจ Ultrasonograms หรือไม่	1. มี 2. ไม่มี	
qm 058	ถ้ามี ผู้ป่วยมีอาการน้ำท่วมปอด หรือไม่	1. มี 2. ไม่มี	
qm 059	ผู้ป่วยมีอาการตับโต (liver enlargement) หรือ น้ำในช่องท้อง (Ascitis) หรือไม่	1. มี 2. ไม่มี	
qm 060	ผู้ป่วยได้รับการตรวจหา เชื้อ ถ้ามี ผล Serotype.....	1. มี 2. ไม่มี	

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## เอกสารคำอธิบายโครงการวิจัยแก่ผู้เข้าร่วมโครงการ

(สำหรับผู้ป่วยไข้เลือดออก)

### โครงการวิจัยเรื่อง

“ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออกในโรงพยาบาลขอนแก่น ประเทศไทย” การศึกษานี้เป็นส่วนหนึ่งของการเรียนในหลักสูตรวิทยาศาสตรมหาบัณฑิต (สาธารณสุขศาสตร์) สาขาโรคติดเชื้อและวิทยาการระบาด ของนางสาวศิริญาพร ชันทะสอน

### วัตถุประสงค์และวิธีการวิจัย

เพื่อศึกษาถึงปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกที่มารับการรักษากลายเป็นผู้ป่วยในที่โรงพยาบาลขอนแก่น

### เหตุผลในการศึกษาวิจัยของโครงการวิจัยนี้

การระบาดของโรคไข้เลือดออกในประเทศไทย ปัจจุบันสามารถพบได้ในหลายจังหวัด พบได้ในทุกกลุ่มอายุ การควบคุมป้องกันโรคจะประสบผลสำเร็จอยู่ที่พฤติกรรมที่ถูกต้องโดยไม่มีพฤติกรรมเสี่ยงที่จะไม่ให้เกิดโรค เช่น การนอนกางมุ้ง การทำลายแหล่งเพาะเชื้อของยุงเป็นต้น แต่ถ้าได้รับเชื้อและเกิดอาการขึ้นแล้วการสังเกตอาการ ดูแลอาการเบื้องต้นง่าย ๆ เป็นสิ่งสำคัญ อย่างยิ่งที่จะสามารถป้องกันโรครุนแรง ก่อนที่จะนำผู้ป่วยไปพบแพทย์ ได้ทันท่วงที อีกทั้งเป็นการป้องกันการช็อกของผู้ป่วยไข้เลือดออก การศึกษานี้จะเป็นประโยชน์ต่อท่านและผู้บุคคลทั่วไปรู้ถึงปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกเพื่อป้องกันการเกิดภาวะช็อก นอกจากนี้ยังเป็นประโยชน์ต่อเจ้าหน้าที่สาธารณสุขในการดูแลรักษาผู้ป่วยป้องกันไม่ให้เกิดภาวะช็อกในผู้ป่วยไข้เลือดออก รวมถึงการรักษาอาการไม่ให้มีอาการรุนแรงจนเกิดการสูญเสียชีวิตเนื่องจากโรคไข้เลือดออก

### เหตุผลที่เชิญชวนให้ท่านเข้าร่วมโครงการวิจัย

ด้วยท่านเป็นผู้ป่วยไข้เลือดออกที่ได้รับการรักษาพยาบาลในโรงพยาบาลขอนแก่น จังหวัดขอนแก่น ผู้วิจัยใคร่ขอเรียนเชิญท่านเข้าร่วมการศึกษาในครั้งนี้เพราะท่านสามารถให้ข้อมูลแก่การวิจัยได้

### สิ่งที่ท่านจะต้องทำและระยะเวลาถ้าท่านตัดสินใจเข้าร่วมการวิจัยนี้

หากท่านตัดสินใจเข้าร่วมการศึกษานี้และลงนามในใบยินยอมแล้ว ท่านจะได้รับการสัมภาษณ์จากผู้วิจัยถึงข้อมูลส่วนบุคคลและข้อมูลการเจ็บป่วย อาการ จากโรคไข้เลือดออกของท่านตั้งแต่เริ่มมีอาการจนถึงเวลาที่เริ่มเข้ารับการรักษาในโรงพยาบาล ซึ่งจะใช้เวลาประมาณ 20 – 25 นาที และ

ผู้วิจัยขออนุญาตที่จะใช้ข้อมูลการเจ็บป่วย การรักษา ของท่านจากเวชระเบียนในโรงพยาบาลเมื่อทาง  
โรงพยาบาลอนุญาต

### **ประโยชน์ของการวิจัยที่คาดว่าจะเกิดต่อตัวท่านและผู้อื่น**

ท่านได้มีส่วนร่วมในงานวิจัยและผลจากการวิจัยเรื่องนี้จะเป็ประโยชน์อย่างยิ่งต่อการ  
เสนอแนะเพื่อการป้องกันการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกและรวมถึงการรักษาผู้ป่วยไข้เลือดออก  
อย่างถูกต้องและรวดเร็วเพื่อไม่ให้ผู้ป่วยไข้เลือดออกมีอาการรุนแรงและถึงแก่การเสียชีวิตเนื่องจากการ  
เกิดภาวะช็อกในผู้ป่วยไข้เลือดออก

### **ความไม่สบายและไม่สะดวกที่อาจจะเกิดขึ้นกับท่านในระหว่างการเข้าร่วมการศึกษาวิจัย**

ในระหว่างการสัมภาษณ์ท่านอาจจะรู้สึกอึดอัดบ้างที่จะต้องตอบคำถามหรือต้องใช้เวลาใน  
การคิดถึงคำตอบที่ใกล้เคียงความจริงที่สุด ท่านสามารถใช้เวลาตามที่ท่านต้องการ หากท่านมีปัญหาใด  
เกี่ยวกับข้อคำถามในแบบสัมภาษณ์ ท่านสามารถสอบถามจากผู้ทำการสัมภาษณ์ได้ และหากท่านไม่ยินดี  
ที่จะตอบ ท่านมีสิทธิที่จะไม่ตอบ และ/หรือ ยุติการสัมภาษณ์ได้ โดยการปฏิเสธดังกล่าว

### **ขอบเขตการดูแลรักษาความลับของท่านในการให้ข้อมูล**

ในการวิจัยครั้งนี้ ข้อมูลทั้งหมดที่ได้รับจากท่านจะได้รับการปกปิดไม่เปิดเผยชื่อในลักษณะ  
ของรายบุคคล จะเปิดเผยได้เฉพาะในรูปแบบที่เป็นผลสรุปในภาพรวมเท่านั้น โดยแบบเก็บข้อมูลจะถูก  
ทำลายทันทีหลังจากการทำวิจัยเสร็จสิ้นแล้ว

### **สิทธิของท่านในการตัดสินใจเข้าร่วมการวิจัยนี้**

ท่านมีสิทธิที่จะตอบรับหรือปฏิเสธการเข้าร่วมวิจัยครั้งนี้ และถึงแม้ท่านได้ยินยอมเข้าร่วมใน  
การวิจัยแล้ว ท่านยังมีสิทธิยกเลิกการเข้าร่วมการวิจัยได้ตลอดเวลา โดยจะไม่ได้มีผลกระทบใดๆ ต่อการ  
ได้รับบริการการรักษาที่ท่านได้รับอยู่ในขณะนี้ และต่อคนในครอบครัวของท่าน ก่อนที่ท่านจะลงชื่อใน  
แบบแสดงความยินยอมเข้าร่วมการวิจัยนี้ ขอให้ท่านแน่ใจว่าได้รับคำตอบ หรือคำอธิบายในข้อที่ท่าน  
สงสัยจนเป็นที่พอใจจากผู้วิจัย

### **หากท่านมีข้อสงสัยเกี่ยวกับการวิจัยครั้งนี้ ท่านสามารถสอบถามได้ที่**

นางสาวศิริญาพร ชันทะสอน

420/1 คณะสาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล อาคาร 7 ชั้น 5

เขตราชวิถี แขวงทุ่งพญาไท กทม. 10400

โทรศัพท์ 089-7971024 โทรสาร 02-6409853

**เอกสารคำอธิบายโครงการวิจัยแก่ผู้เข้าร่วมโครงการ**  
**(สำหรับผู้ป่วยไข้เลือดออกที่มารับการรักษาเป็นผู้ป่วยในที่โรงพยาบาลขอนแก่น**  
**ที่เป็นเด็กและสามารถอ่านหนังสือได้โดยมีอายุน้อยกว่า 20 ปี)**  
**โครงการวิจัยเรื่อง**

“ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออกในโรงพยาบาลขอนแก่น ประเทศไทย” การศึกษานี้เป็นส่วนหนึ่งของการเรียนในหลักสูตรวิทยาศาสตรมหาบัณฑิต (สาธารณสุขศาสตร์) สาขาโรคติดเชื้อและวิทยาการระบาด ของผู้วิจัยชื่อศิริญาพร ชันทะสอน

**วัตถุประสงค์และวิธีการวิจัย**

เพื่อศึกษาถึงปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกที่มารับการรักษาเป็นผู้ป่วยในที่โรงพยาบาลขอนแก่น

**เหตุผลในการศึกษาวิจัยของโครงการวิจัยนี้**

ตามที่หนูทราบกันดีแล้วว่าโรคไข้เลือดออกนั้นเป็นโรคที่พบได้ทุกจังหวัดในประเทศไทย และพบได้ในทุกกลุ่มอายุ การควบคุมป้องกันโรคนี้ได้แก่ การนอนกางมุ้ง การทำลายแหล่งเพาะเชื้อของยุงเป็นต้น แต่ถ้ายุงกัดและเกิดอาการขึ้นแล้วการสังเกตอาการและดูแลอาการเบื้องต้นง่ายๆ เป็นสิ่งสำคัญอย่างมากที่จะสามารถป้องกันโรคนี้ไม่ให้รุนแรง ก่อนที่จะนำผู้ป่วยไปพบหมอรักษาได้ทันที่ ทั้งทั้งเป็นการป้องกันการช็อกของผู้ป่วยไข้เลือดออก การศึกษานี้จะเป็นประโยชน์ต่อตัวหนูเองและผู้อื่นให้รู้ถึงปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกเพื่อป้องกันการเกิดภาวะช็อก นอกจากนี้ยังเป็นประโยชน์ต่อหมอและพยาบาลในการดูแลรักษาผู้ป่วยป้องกันไม่ให้เกิดภาวะช็อกในผู้ป่วยไข้เลือดออกรวมถึงการรักษาอาการไม่ให้มีอาการรุนแรงจนเกิดการตายเนื่องจากโรคไข้เลือดออก

**เหตุผลที่เชิญชวนให้หนูเข้าร่วมโครงการวิจัย**

ด้วยหนูป่วยเป็นโรคไข้เลือดออกที่ได้รับการรักษาพยาบาลในโรงพยาบาลขอนแก่น จังหวัดขอนแก่น พี่ผู้วิจัยขอชวนหนูเข้าร่วมการศึกษาในครั้งนี้เพราะหนูสามารถให้ข้อมูลแก่การวิจัยได้

**สิ่งที่หนูจะต้องทำและระยะเวลา ถ้าหนูตัดสินใจเข้าร่วมการวิจัยนี้**

หากหนูเต็มใจเข้าร่วมการศึกษานี้หลังจากปรึกษาคุณพ่อ คุณแม่หรือผู้ปกครองของหนู และลงชื่อในใบยินยอมแล้ว หนูจะได้รับการสัมภาษณ์จากพี่ผู้วิจัยถึงข้อมูลส่วนตัวและข้อมูลอาการไม่สบายจากโรคไข้เลือดออกของหนูตั้งแต่เริ่มมีไข้จนถึงเวลาที่เริ่มเข้ารับการรักษาในโรงพยาบาล ซึ่งจะใช้

ระยะเวลาประมาณ 20 – 25 นาที และที่ผู้วิจัยขออนุญาตที่จะใช้ข้อมูลการเจ็บป่วย การรักษา ของหนูจากเวชระเบียนในโรงพยาบาลเมื่อทางโรงพยาบาลอนุญาต

### **ประโยชน์ของการวิจัยที่คาดว่าจะเกิดต่อตัวหนูและผู้อื่น**

หนูจะ ได้มีส่วนร่วมในงานวิจัยและผลจากการวิจัยเรื่องนี้จะ เป็นประโยชน์ต่อการการป้องกัน การเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกและรวมถึงการรักษาผู้ป่วยไข้เลือดออกอย่างถูกต้องและรวดเร็ว เพื่อไม่ให้ผู้ป่วยไข้เลือดออกมีอาการรุนแรงและตายเนื่องจากการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออก

### **ความไม่สบายและไม่สะดวกที่อาจจะเกิดขึ้นกับหนูระหว่างการเข้าร่วมการศึกษาวิจัย**

ในระหว่างการสัมภาษณ์หนูอาจจะรู้สึกอึดอัดบ้างที่จะต้องตอบคำถามหรือต้องใช้เวลาในการนึกคำตอบที่ใกล้เคียงความจริงที่สุด หนูสามารถใช้เวลาตามที่หนูต้องการ หากหนูมีปัญหาใดเกี่ยวกับข้อคำถามในแบบสัมภาษณ์ที่หนูไม่เข้าใจ หนูสามารถสอบถามเพิ่มเติมจากที่ผู้ทำการสัมภาษณ์ได้ และหากหนูไม่อยากจะตอบ หนูมีสิทธิที่จะไม่ตอบ และ/หรือ หยุดการสัมภาษณ์ได้ โดยไม่มีใครโกรธและทำโทษ หนู คุณหมอและคุณพยาบาลจะดูแลและรักษาหนูเหมือนเดิม

### **ขอบเขตการดูแลรักษาความลับของหนูในการให้ข้อมูล**

ในการวิจัยครั้งนี้ข้อมูลทั้งหมดที่ได้รับจากหนูจะได้รับการปกปิดเป็นความลับโดยจะไม่เปิดเผยชื่อของหนู จะเปิดเผยเฉพาะข้อมูลที่เป็นผลสรุปในภาพรวมเท่านั้น โดยแบบเก็บข้อมูลจะถูกทำลายทันทีหลังจากการทำวิจัยเสร็จสิ้นแล้ว

### **สิทธิของหนูในการตัดสินใจเข้าร่วมการวิจัยนี้**

หนูมีสิทธิเลือกที่จะเข้าร่วมหรือไม่เข้าร่วมวิจัยครั้งนี้หลังจากที่หนูได้ปรึกษาคุณพ่อและคุณแม่หรือผู้ปกครองของหนูแล้ว และถึงแม้หนูได้ยินยอมเข้าร่วมในการวิจัยแล้ว หนูยังมีสิทธิยกเลิกการเข้าร่วมการวิจัยได้ตลอดเวลา ก่อนที่หนูจะลงชื่อในแบบแสดงความยินยอมเข้าร่วมการวิจัยนี้ ขอให้หนูแน่ใจว่าได้รับคำตอบ หรือคำอธิบายในข้อที่หนูสงสัยจนเป็นที่พอใจจากที่ผู้วิจัยแล้ว

### **หากหนูมีข้อสงสัยเกี่ยวกับการวิจัยครั้งนี้ หนูสามารถสอบถามได้ที่**

นางสาวศิริญาพร ชันทะสอน (พี่เอ๋)

420/1 คณะสาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล อาคาร 7 ชั้น 5

เขตราชวิถี แขวงทุ่งพญาไท กทม. 10400

โทรศัพท์ 089-7971024 โทรสาร 02-6409853

## เอกสารคำอธิบายโครงการวิจัยแก่ผู้เข้าร่วมโครงการ

(สำหรับผู้ดูแลผู้ป่วย)

### โครงการวิจัยเรื่อง

“ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออกในโรงพยาบาลขอนแก่น ประเทศไทย” การศึกษานี้เป็นส่วนหนึ่งของการเรียนในหลักสูตรวิทยาศาสตรมหาบัณฑิต (สาธารณสุขศาสตร์) สาขาโรคติดเชื้อและวิทยาการระบาด ของนางสาวศิริญาพร จันทร์สอน

### วัตถุประสงค์และวิธีการวิจัย

เพื่อศึกษาปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกที่มารับการรักษาเป็นผู้ป่วยในที่โรงพยาบาลขอนแก่น

### เหตุผลในการศึกษาวิจัยของโครงการวิจัยนี้

การระบาดของโรคไข้เลือดออกในประเทศไทย ปัจจุบันสามารถพบได้ในหลายจังหวัด พบได้ในทุกกลุ่มอายุ การควบคุมป้องกันโรคจะประสบผลสำเร็จอยู่ที่พฤติกรรมที่ถูกต้องโดยไม่มีพฤติกรรมเสี่ยงที่จะไม่ให้เกิดโรค เช่น การนอนกางมุ้ง การทำลายแหล่งเพาะเชื้อของยุงเป็นต้น แต่ถ้าได้รับเชื้อและเกิดอาการขึ้นแล้วการสังเกตอาการ ดูแลอาการเบื้องต้นง่าย ๆ เป็นสิ่งสำคัญ อย่างยิ่งที่จะสามารถป้องกันโรคไม่ให้รุนแรง ก่อนที่จะนำผู้ป่วยไปพบแพทย์ ได้ทันเวลาที่ อีกทั้งเป็นการป้องกันการช็อกของคนไข้ การศึกษานี้จะเป็นประโยชน์ต่อท่านและผู้บุคคลทั่วไปรู้ถึงปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกเพื่อป้องกันการเกิดภาวะช็อก นอกจากนี้ยังเป็นประโยชน์ต่อเจ้าหน้าที่สาธารณสุขในการดูแลรักษาผู้ป่วยป้องกันไม่ให้เกิดภาวะช็อกในผู้ป่วยไข้เลือดออก รวมถึงการรักษาอาการไม่ให้มีอาการรุนแรงจนเกิดการสูญเสียชีวิตเนื่องจากโรคไข้เลือดออก

### เหตุผลที่เชิญชวนท่านให้เข้าร่วมในโครงการวิจัยนี้

ด้วยท่านเป็นผู้ดูแลผู้ป่วยไข้เลือดออกที่เข้ารับการรักษาพยาบาลในโรงพยาบาลขอนแก่น จังหวัดขอนแก่น ผู้วิจัยใคร่ขอเรียนเชิญท่านเข้าร่วมการศึกษาในครั้งนี้เพราะท่านสามารถให้ข้อมูลแก่การวิจัยได้

### สิ่งที่ท่านจะต้องทำและระยะเวลาถ้าท่านตัดสินใจเข้าร่วมการศึกษาวินิจฉัยครั้งนี้

หากท่านตัดสินใจเข้าร่วมการศึกษาวินิจฉัยครั้งนี้และลงนามในใบยินยอมแล้ว ท่านจะได้รับการสัมภาษณ์จากผู้วิจัยเกี่ยวกับข้อมูลส่วนบุคคลของท่าน ข้อมูลการเจ็บป่วย และอาการของผู้ป่วยก่อนที่จะเข้ารับการรักษาในโรงพยาบาลที่เป็นญาติของท่าน ซึ่งจะใช้เวลาประมาณ 20 – 25 นาที นอกจากนั้น

ผู้วิจัยขออนุญาตผู้ป่วยที่จะใช้ข้อมูลและการรักษาของผู้ป่วยไข้เลือดออกที่เป็นญาติของท่านและท่านได้ดูแลก่อนเข้ารับการรักษาในโรงพยาบาลนี้จากเวชระเบียนของโรงพยาบาลเมื่อได้รับอนุญาตจากทางโรงพยาบาล

### **ประโยชน์ของการวิจัยที่คาดว่าจะเกิดต่อตัวท่านและผู้อื่น**

ท่านได้มีส่วนร่วมในงานวิจัยและผลจากการวิจัยเรื่องนี้จะประโยชน์อย่างยิ่งต่อการเสนอแนะเพื่อการป้องกันการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออกและรวมถึงการรักษาผู้ป่วยไข้เลือดออกอย่างถูกต้องและรวดเร็วเพื่อไม่ให้ผู้ป่วยไข้เลือดออกมีอาการรุนแรงและถึงแก่การเสียชีวิตเนื่องจากการเกิดภาวะช็อกในผู้ป่วยไข้เลือดออก

### **ความไม่สบายและไม่สะดวกที่อาจจะเกิดขึ้นจากการเข้าร่วมการศึกษาวิจัย**

ในระหว่างการสัมภาษณ์ท่านอาจจะรู้สึกอึดอัดบ้างที่จะต้องตอบคำถามหรือต้องใช้เวลาในการคิดถึงคำตอบที่ใกล้เคียงความจริงที่สุด ท่านสามารถใช้เวลาตามที่ท่านต้องการ หากท่านมีปัญหาใดเกี่ยวกับข้อคำถามในแบบสัมภาษณ์ ท่านสามารถสอบถามจากผู้ทำการสัมภาษณ์ได้ และหากท่านไม่ยินดีที่จะตอบ ท่านมีสิทธิที่จะไม่ตอบ และ/หรือ ยุติการสัมภาษณ์ได้ โดยการปฏิเสธดังกล่าว

### **ขอบเขตการดูแลรักษาความลับของข้อมูลต่างๆ ของท่านเมื่อท่านตัดสินใจเข้าร่วมการวิจัย**

ในการวิจัยครั้งนี้ ข้อมูลทั้งหมดที่ได้รับจากท่านจะได้รับการปกปิดไม่เปิดเผยชื่อในลักษณะของรายบุคคล จะเปิดเผยได้เฉพาะในรูปแบบที่เป็นผลสรุปในภาพรวมเท่านั้น โดยแบบเก็บข้อมูลจะถูกทำลายทันทีหลังจากการทำวิจัยเสร็จสิ้นแล้ว

### **สิทธิของท่านในการตัดสินใจเข้าร่วมการวิจัยนี้**

ท่านมีสิทธิที่จะตอบรับหรือปฏิเสธการเข้าร่วมวิจัยครั้งนี้ และถึงแม้ท่านได้ยินยอมเข้าร่วมในการวิจัยแล้ว ท่านยังมีสิทธิยกเลิกการเข้าร่วมการวิจัยได้ตลอดเวลา โดยจะไม่ได้มีผลกระทบใดๆ ต่อการได้รับบริการการรักษาที่ท่านได้รับอยู่ในขณะนี้ และต่อคนในครอบครัวของท่าน ก่อนที่ท่านจะลงชื่อในแบบแสดงความยินยอมเข้าร่วมการวิจัยนี้ ขอให้ท่านแน่ใจว่าได้รับได้รับคำตอบ หรือคำอธิบายในข้อที่ท่านสงสัยจนเป็นที่พอใจจากผู้วิจัย

### **หากท่านมีข้อสงสัยเกี่ยวกับการวิจัยครั้งนี้ ท่านสามารถสอบถามได้ที่**

นางสาวศิริญาพร ชันทะสอน

420/1 คณะสาธารณสุขศาสตร์ มหาวิทยาลัยมหิดล อาคาร 7 ชั้น 5

เขตราชวิถี แขวงทุ่งพญาไท กทม. 10400

โทรศัพท์ 089-7971024 โทรสาร 02-6409853

**ใบยินยอมเข้าร่วมวิจัยของผู้เข้าร่วมโครงการ  
สำหรับผู้ป่วยไข้เลือดออกที่มารับการรักษาเป็นผู้ป่วยในที่โรงพยาบาลขอนแก่น**

ทำที่.....

วันที่.....

ข้าพเจ้า.....อายุ.....ปี อยู่บ้านเลขที่.....

ถนน.....หมู่ที่.....แขวง/ตำบล.....เขต/อำเภอ.....จังหวัด.....

ขอทำหนังสือนี้ไว้ต่อผู้วิจัยเพื่อเป็นหลักฐานแสดงว่า

ข้อ 1. ข้าพเจ้าได้รับทราบการศึกษาวิจัยของ (ผู้วิจัย) นางสาวศิริญาพร ชันทะสอน เรื่อง ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออกในโรงพยาบาลขอนแก่น ประเทศไทย

ข้อ 2. ข้าพเจ้ายินยอมเข้าร่วมโครงการวิจัยนี้ด้วยความสมัครใจ โดยมิได้มีการบังคับ ชูเชิญ หลอกลวงแต่ประการใด

ข้อ 3. ข้าพเจ้าได้รับการอธิบายจากผู้วิจัยเกี่ยวกับวัตถุประสงค์ของการวิจัย วิธีการวิจัย รวมทั้งประโยชน์ที่จะได้รับจากการวิจัยโดยละเอียดไม่มีสิ่งใดปกปิดซ่อนเร้นแล้วจากเอกสารโครงการวิจัย

ข้อ 4. ข้าพเจ้าได้รับการรับรองจากผู้วิจัยว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ จะเปิดเผยเฉพาะผลสรุปการวิจัยเท่านั้น

ข้อ 5. ข้าพเจ้าได้อ่านและทำความเข้าใจข้อมูลทั้งหมดในเอกสารคำแนะนำสำหรับผู้เข้าร่วมโครงการวิจัยนี้แล้ว และข้าพเจ้าได้ซักถามปัญหาที่ข้องใจจนเป็นที่พอใจแล้ว

ข้อ 6. ข้าพเจ้าได้รับทราบแล้วว่าข้าพเจ้ามีสิทธิ์จะบอกเลิกการร่วมโครงการวิจัยนี้ก่อนเริ่มการวิจัยและการบอกเลิกการร่วมโครงการวิจัยจะไม่มีผลกระทบต่อการศึกษาโรคที่ข้าพเจ้าจะพึงได้รับต่อไป

ข้อ 7. นางสาวศิริญาพร ชันทะสอน ผู้วิจัย ได้เขียนบรรยายเกี่ยวกับรายละเอียดต่าง ๆ ของโครงการ ตลอดจนประโยชน์ของการวิจัยนี้ ให้ข้าพเจ้าทราบ

ข้าพเจ้าได้อ่านและเข้าใจข้อความตามหนังสือนี้โดยตลอดแล้ว เห็นว่าถูกต้องตามเจตนาของข้าพเจ้า จึงได้ลงลายมือชื่อไว้เป็นสำคัญพร้อมกับหัวหน้าผู้วิจัยและต่อหน้าพยาน

ลงชื่อ.....ผู้ยินยอม/ผู้ปกครอง/ผู้แทนอันชอบธรรม

(.....)

ลงชื่อ.....ผู้วิจัย

(.....)

ลงชื่อ.....พยาน

(.....)

ลงชื่อ.....พยาน

(.....)

หมายเหตุ

- 0) ในกรณีผู้ให้ความยินยอมมีอายุไม่ครบ 20 ปีบริบูรณ์ จะต้องเป็นผู้ปกครองตามกฎหมายเป็นผู้ให้ความยินยอมด้วย
- 0) ขออนขอมนี้ให้แก่ผู้ยินยอมตนให้ทำการวิจัยฟังจนเข้าใจดีแล้ว และให้ผู้ยินยอมตนให้ทำวิจัยลงนาม หรือพิมพ์ลายนิ้วหัวแม่มือรับทราบในการให้ความยินยอมดังกล่าวด้วย

**ใบยินยอมเข้าร่วมวิจัยของผู้เข้าร่วมโครงการ**  
**สำหรับผู้ป่วยไข้เลือดออกที่มารับการรักษาเป็นผู้ป่วยในที่โรงพยาบาลขอนแก่น**  
**ที่เป็นเด็กและสามารถอ่านหนังสือได้โดยมีอายุน้อยกว่า 20 ปี**  
**ให้ลงลายมือชื่อใน Assent form**

ทำที่.....

วันที่.....

ชื่อของผู้เยาว์.....อายุ.....ปี อยู่บ้านเลขที่.....

ถนน.....หมู่ที่.....แขวง/ตำบล.....เขต/อำเภอ.....จังหวัด.....

หนูขอทำหนังสือนี้ให้ไว้ต่อที่ผู้วิจัยเพื่อเป็นหลักฐานแสดงว่า

1. หนูจะเข้าร่วมการวิจัยครั้งนี้เนื่องจากหนูไม่สบายและนอนในโรงพยาบาลด้วยโรคไข้เลือดออก การวิจัยนี้ทำเพื่อดูว่าปัจจัยอะไรที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออกในโรงพยาบาลขอนแก่น

- 0. หนูเต็มใจที่จะเข้าร่วมการวิจัยนี้โดยไม่มีใครบังคับให้หนูเข้าร่วมโครงการนี้แต่อย่างใด
- 0. หนูได้รับการรับรองจากที่ผู้วิจัยว่าจะเก็บข้อมูลของหนูเป็นความลับ
- 0. หนูได้รับการอธิบายรายละเอียดของโครงการนี้จากที่ผู้วิจัยแล้ว
- 0. หนูสามารถที่จะไม่เข้าร่วมโครงการวิจัยนี้ได้หากหนูไม่ต้องการ โดยที่พ่อ แม่หรือผู้ปกครอง จะไม่โกรธและไม่ทำโทษหนู คุณหมอและคุณพยาบาลจะดีกับหนูและรักษาหนูเหมือนเดิม

ที่ผู้วิจัยครั้งนี้คือ นางสาวศิริญาพร ชันทะสอน (พี่เอ๋) ได้เขียนอธิบายรายละเอียดต่าง ๆ ของโครงการและประโยชน์ของการวิจัยนี้ให้หนูได้ทราบแล้ว

หนูเข้าใจในสิ่งที่พูดมาทั้งหมดแล้ว และการยินยอมของหนูทำได้โดยลงชื่อในช่องผู้เยาว์ข้างล่างนี้

ลงชื่อ.....ผู้เยาว์

(.....)

ลงชื่อ.....ผู้วิจัย

(.....)

ลงชื่อ.....พยาน

(.....)

ลงชื่อ.....พยาน

(.....)

หมายเหตุ

- 0) ในกรณีผู้ให้ความยินยอมมีอายุไม่ครบ 20 ปีบริบูรณ์ จะต้องเป็นผู้ปกครองตามกฎหมายเป็นผู้ให้ความยินยอมด้วย
- 0) กรณีผู้ยินยอมคนให้ทำวิจัยไม่สามารถอ่านหนังสือได้ ให้ผู้วิจัยอ่านข้อความในหนังสือให้ความยินยอมนี้ให้แก่ผู้ยินยอมคนให้ทำการวิจัยฟังจนเข้าใจดีแล้ว และให้ผู้ยินยอมคนให้ทำวิจัยลงนามหรือพิมพ์ลายนิ้วหัวแม่มือรับทราบในการให้ความยินยอมดังกล่าวด้วย

## ใบยินยอมเข้าร่วมวิจัยของผู้เข้าร่วมโครงการ

### ผู้ดูแลผู้ป่วย

ทำที่.....

วันที่.....

ข้าพเจ้า.....อายุ.....ปี อยู่บ้านเลขที่.....

ถนน.....หมู่ที่.....แขวง/ตำบล.....เขต/อำเภอ.....จังหวัด.....

ขอทำหนังสือนี้ไว้ต่อผู้วิจัยเพื่อเป็นหลักฐานแสดงว่า

ข้อ 1. ข้าพเจ้าได้รับทราบการศึกษาวิจัยของ (ผู้วิจัย) นางสาวศิริญาพร ชันทะสอน เรื่อง ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออกในโรงพยาบาลขอนแก่น ประเทศไทย

ข้อ 2. ข้าพเจ้ายินยอมเข้าร่วมโครงการวิจัยนี้ด้วยความสมัครใจ โดยมิได้มีการบังคับ ชูเชื้อ หลอกลวงแต่ประการใด

ข้อ 3. ข้าพเจ้าได้รับการอธิบายจากผู้วิจัยเกี่ยวกับวัตถุประสงค์ของการวิจัย วิธีการวิจัย รวมทั้งประโยชน์ที่จะได้รับจากการวิจัยโดยละเอียดไม่มีสิ่งใดปกปิดซ่อนเร้นแล้วจากเอกสาร โครงการวิจัย

ข้อ 4. ข้าพเจ้าได้รับการรับรองจากผู้วิจัยว่าจะเก็บข้อมูลส่วนตัวของข้าพเจ้าเป็นความลับ จะเปิดเผยเฉพาะผลสรุปการวิจัยเท่านั้น

ข้อ 5. ข้าพเจ้าได้อ่านและทำความเข้าใจข้อมูลทั้งหมดในเอกสารคำแนะนำสำหรับผู้เข้าร่วมโครงการวิจัยนี้แล้ว และข้าพเจ้าได้ซักถามปัญหาที่ข้องใจจนเป็นที่พอใจแล้ว

ข้อ 6. ข้าพเจ้าได้รับทราบแล้วว่าข้าพเจ้ามีสิทธิ์จะบอกเลิกการร่วมโครงการวิจัยนี้ก่อนเริ่มการวิจัยและการบอกเลิกการร่วมโครงการวิจัยจะไม่มีผลกระทบต่อการศึกษาโรคที่ข้าพเจ้าจะพึงได้รับต่อไป

ข้อ 7. นางสาวศิริญาพร ชันทะสอน ผู้วิจัย ได้เขียนบรรยายเกี่ยวกับรายละเอียดต่าง ๆ ของโครงการ ตลอดจนประโยชน์ของการวิจัยนี้ให้ข้าพเจ้าทราบ

ข้าพเจ้าได้อ่านและเข้าใจข้อความตามหนังสือนี้โดยตลอดแล้ว เห็นว่าถูกต้องตามเจตนาของข้าพเจ้า จึงได้ลงลายมือชื่อไว้เป็นสำคัญพร้อมกับหัวหน้าผู้วิจัยและต่อหน้าพยาน

ลงชื่อ.....ผู้ยินยอม/ผู้ปกครอง/ผู้แทนอันชอบธรรม

(.....)

ลงชื่อ.....ผู้วิจัย

(.....)

ลงชื่อ.....พยาน

(.....)

ลงชื่อ.....พยาน

(.....)

หมายเหตุ

- 0) ในกรณีผู้ให้ความยินยอมมีอายุไม่ครบ 20 ปีบริบูรณ์ จะต้องเป็นผู้ปกครองตามกฎหมายเป็นผู้ให้ความยินยอมด้วย
- 2) กรณีผู้ยินยอมคนให้ทำวิจัยไม่สามารถอ่านหนังสือได้ ให้ผู้วิจัยอ่านข้อความในหนังสือให้ความยินยอมนี้ให้แก่ผู้ยินยอมคนให้ทำการวิจัยฟังจนเข้าใจดีแล้ว และให้ผู้ยินยอมคนให้ทำวิจัยลงนามหรือพิมพ์ลายนิ้วหัวแม่มือรับทราบในการให้ความยินยอมดังกล่าวด้วย

### APPENDIX C



No. MU 2007-072

**Documentary Proof of Ethical Clearance  
The Committee on Human Rights Related to  
Human Experimentation  
Mahidol University, Bangkok**


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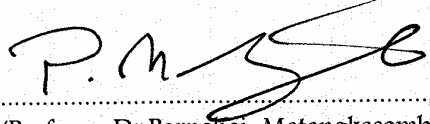
**Title of Project:** Factors Related to Stage of Shock among Patients with Dengue in Khon-Kaen Hospital, Thailand  
(Thesis for Master Degree)

**Principle Investigator:** Miss Siriyaporn Khuntason

**Name of Institution:** Faculty of Public Health

**Approved by the Committee on Human Rights Related to Human Experimentation**

**Signature of Chairman:** .....   
(Professor Dr. Srisin Khusmith)

**Signature of Head of the Institute:** .....   
(Professor Dr. Pornchai Matangkasombut)

**Date of Approval:** ..... 12 APR 2007

**Date of Expiration:** ..... 1.1 APR 2008

ใบรับรองจริยธรรมทางการวิจัย โรงพยาบาลขอนแก่น (จ.4)



เอกสารรับรองจริยธรรมทางการวิจัย

เอกสารฉบับนี้ เพื่อแสดงว่า โครงการวิจัย

เรื่อง ปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะช็อกของผู้ป่วยไข้เลือดออกในโรงพยาบาลขอนแก่น ประเทศไทย  
(Factors Related to Shock among Dengue Patients in Khon-Kaen Hospital, Thailand)

ผู้วิจัย คือ นางสาวศิริญาพร ชันทะสอน และคณะ

สถาบัน/หน่วยงาน นักศึกษาระดับปริญญาโท มหาวิทยาลัยมหิดล หลักสูตรปริญญาโท  
สาขาวิชาเอกโรคติดเชื้อและวิทยาการระบาด คณะสาธารณสุขศาสตร์

ได้ผ่านการพิจารณาจากคณะกรรมการจริยธรรมทางการวิจัย โรงพยาบาลขอนแก่น แล้ว  
และเห็นว่าผู้วิจัยต้องดำเนินการตามโครงการวิจัยที่ได้กำหนดไว้แล้ว หากจะมีการปรับเปลี่ยนหรือ  
แก้ไขใด ๆ ควรผ่านความเห็นชอบหรือแจ้งต่อคณะกรรมการจริยธรรมทางการวิจัยอีกครั้ง

ออกให้ ณ วันที่ 2๒ เดือน เมษายน พ.ศ. 2550

ลงชื่อ .....

(นายสมศักดิ์ ประมุขภาณวัตร)

นายแพทย์ 8

ประธานกรรมการจริยธรรมทางการวิจัย

โรงพยาบาลขอนแก่น

ลงชื่อ .....

(นายวิทยา จารุพูนผล)

ผู้อำนวยการโรงพยาบาลขอนแก่น



คณะกรรมการ  
จริยธรรมวิจัยในมนุษย์  
รพ.ขอนแก่น

ลำดับที่ 17/02/2550

คณะกรรมการจริยธรรมทางการวิจัย โรงพยาบาลขอนแก่น

สำนักงาน: งานวิจัยและพัฒนาระบบสุขภาพ กลุ่มพัฒนาระบบบริการสุขภาพ โรงพยาบาลขอนแก่น

ถนนศรีจันทร์ อำเภอเมือง จังหวัดขอนแก่น 40000

โทร. (043) 336789 ต่อ 1160 โทรสาร (043) 337053



**ตารางที่ 3 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์ความยาว (สำหรับเด็กอายุต่ำกว่า 2 ปี)**

ความยาว (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)						เพศหญิง : น้ำหนัก (กิโลกรัม)					
	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < - 1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ทั่ว > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < - 1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ทั่ว > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.
50	2.6	2.7 - 2.7	2.8 - 3.8	3.9 - 3.9	4.0 - 4.1	4.2	2.6	2.7 - 2.7	2.8 - 3.8	3.9 - 3.9	4.0 - 4.2	4.3
51	2.8	2.9 - 3.0	3.1 - 4.0	4.1 - 4.2	4.3 - 4.4	4.5	2.5	2.9 - 2.9	3.0 - 4.1	4.2 - 4.2	4.3 - 4.5	4.6
52	3.0	3.1 - 3.2	3.3 - 4.3	4.4 - 4.5	4.6 - 4.6	4.9	3.0	3.1 - 3.2	3.3 - 4.3	4.4 - 4.5	4.6 - 4.8	4.9
53	3.2	3.3 - 3.4	3.5 - 4.6	4.7 - 4.7	4.8 - 5.1	5.2	3.2	3.3 - 3.4	3.5 - 4.6	4.7 - 4.8	4.9 - 5.1	5.2
54	3.4	3.5 - 3.6	3.7 - 4.9	5.0 - 5.0	5.1 - 5.4	5.5	3.4	3.5 - 3.6	3.7 - 4.9	5.0 - 5.0	5.1 - 5.4	5.5
55	3.6	3.7 - 3.8	3.9 - 5.1	5.2 - 5.3	5.4 - 5.7	5.8	3.6	3.7 - 3.8	3.9 - 5.1	5.2 - 5.3	5.4 - 5.7	5.8
56	3.9	4.0 - 4.1	4.2 - 5.4	5.5 - 5.6	5.7 - 6.0	6.1	3.8	3.9 - 4.0	4.1 - 5.4	5.5 - 5.6	5.7 - 6.0	6.1
57	4.1	4.2 - 4.3	4.4 - 5.7	5.8 - 5.9	6.0 - 6.3	6.4	4.0	4.1 - 4.2	4.3 - 5.6	5.7 - 5.9	6.0 - 6.3	6.4
58	4.3	4.4 - 4.5	4.6 - 6.0	6.1 - 6.2	6.3 - 6.6	6.7	4.2	4.3 - 4.4	4.5 - 5.9	6.0 - 6.1	6.2 - 6.6	6.7
59	4.5	4.6 - 4.8	4.9 - 6.3	6.4 - 6.5	6.6 - 6.9	7.0	4.4	4.5 - 4.7	4.8 - 6.2	6.3 - 6.4	6.5 - 6.9	7.0
60	4.7	4.8 - 5.0	5.1 - 6.6	6.6 - 6.8	6.9 - 7.3	7.4	4.6	4.7 - 4.9	5.0 - 6.4	6.5 - 6.7	6.8 - 7.2	7.3
61	5.0	5.1 - 5.2	5.3 - 6.8	6.9 - 7.1	7.2 - 7.6	7.7	4.8	4.9 - 5.1	5.2 - 6.7	6.8 - 6.9	7.0 - 7.4	7.5
62	5.2	5.3 - 5.4	5.5 - 7.1	7.2 - 7.4	7.5 - 7.9	8.0	5.0	5.1 - 5.3	5.4 - 6.9	7.0 - 7.2	7.3 - 7.7	7.8
63	5.4	5.5 - 5.7	5.8 - 7.4	7.5 - 7.7	7.8 - 8.2	8.3	5.2	5.3 - 5.5	5.6 - 7.2	7.3 - 7.5	7.6 - 8.0	8.1
64	5.6	5.7 - 5.9	6.0 - 7.7	7.8 - 7.9	8.0 - 8.5	8.6	5.4	5.5 - 5.7	5.8 - 7.4	7.5 - 7.7	7.8 - 8.3	8.4

ตารางที่ 3 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์ความยาว (สำหรับเด็กอายุต่ำกว่า 2 ปี)														
ความยาว (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)							เพศหญิง : น้ำหนัก (กิโลกรัม)						
	ห่อม	ค่อนข้างห่อม	สมส่วน	ทั่ว	เริ่มอ้วน	อ้วน	ห่อม	ค่อนข้างห่อม	สมส่วน	ทั่ว	เริ่มอ้วน	อ้วน		
	< - 2 S.D. ถึง < -1.5 S.D.	- 2 S.D. ถึง < -1.5 S.D.	- 1.5 S.D. ถึง + 1.5 S.D.	> + 1.5 S.D. ถึง + 2 S.D.	> + 2 S.D. ถึง + 3 S.D.	> + 3 S.D.	< - 2 S.D. ถึง < -1.5 S.D.	- 2 S.D. ถึง < -1.5 S.D.	- 1.5 S.D. ถึง + 1.5 S.D.	> + 1.5 S.D. ถึง + 2 S.D.	> + 2 S.D. ถึง + 3 S.D.	> + 3 S.D.		
65	5.8	5.9 - 6.1	6.2 - 8.0	8.1 - 8.2	8.3 - 8.8	8.9	5.6	5.7 - 5.9	6.0 - 7.7	7.8 - 8.0	8.1 - 8.5	8.6		
66	6.1	6.2 - 6.4	6.5 - 8.2	8.3 - 8.5	8.6 - 9.1	9.2	5.8	5.9 - 6.1	6.2 - 7.9	8.0 - 8.2	8.3 - 8.8	8.9		
67	6.3	6.4 - 6.6	6.7 - 8.5	8.6 - 8.8	8.9 - 9.4	9.5	6.0	6.1 - 6.3	6.4 - 8.2	8.3 - 8.5	8.6 - 9.1	9.2		
68	6.5	6.6 - 6.8	6.9 - 8.8	8.9 - 9.1	9.2 - 9.7	9.8	6.2	6.3 - 6.5	6.6 - 8.4	8.5 - 8.7	8.8 - 9.3	9.4		
69	6.7	6.8 - 7.0	7.1 - 9.0	9.1 - 9.4	9.5 - 10.0	10.1	6.4	6.6 - 6.7	6.8 - 8.7	8.8 - 9.0	9.1 - 9.6	9.7		
70	6.9	7.0 - 7.3	7.4 - 9.3	9.4 - 9.6	9.7 - 10.3	10.4	6.6	6.7 - 6.9	7.0 - 8.9	9.0 - 9.2	9.3 - 9.9	10.0		
71	7.1	7.2 - 7.5	7.6 - 9.6	9.7 - 9.9	10.0 - 10.5	10.6	6.8	6.9 - 7.1	7.2 - 9.1	9.2 - 9.5	9.6 - 10.1	10.2		
72	7.3	7.4 - 7.7	7.8 - 9.8	9.9 - 10.2	10.3 - 10.8	10.9	7.0	7.1 - 7.3	7.4 - 9.4	9.5 - 9.7	9.8 - 10.4	10.5		
73	7.6	7.7 - 7.9	8.0 - 10.1	10.2 - 10.4	10.5 - 11.1	11.2	7.2	7.3 - 7.5	7.6 - 9.6	9.7 - 10.0	10.1 - 10.6	10.7		
74	7.8	7.9 - 8.1	8.2 - 10.4	10.5 - 10.7	10.8 - 11.4	11.5	7.4	7.5 - 7.7	7.8 - 9.8	9.9 - 10.2	10.3 - 10.9	11.0		
75	8.0	8.1 - 8.4	8.5 - 10.6	10.7 - 11.0	11.1 - 11.7	11.8	7.6	7.7 - 7.9	8.0 - 10.1	10.2 - 10.4	10.5 - 11.1	11.2		
76	8.2	8.3 - 8.6	8.7 - 10.9	11.0 - 11.2	11.3 - 12.0	12.1	7.8	7.9 - 8.1	8.2 - 10.3	10.4 - 10.7	10.8 - 11.4	11.5		
77	8.4	8.5 - 8.8	8.9 - 11.1	11.2 - 11.5	11.6 - 12.3	12.4	8.0	8.1 - 8.3	8.4 - 10.5	10.6 - 10.9	11.0 - 11.6	11.7		
78	8.6	8.7 - 9.0	9.1 - 11.4	11.5 - 11.8	11.9 - 12.6	12.7	8.1	8.2 - 8.5	8.6 - 10.8	10.9 - 11.1	11.2 - 11.8	11.9		
79	8.9	9.0 - 9.2	9.3 - 11.7	11.8 - 12.1	12.2 - 12.9	13.0	8.3	8.4 - 8.7	8.8 - 11.0	11.1 - 11.3	11.4 - 12.1	12.2		

**ตารางที่ 3 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์ความยาว (สำหรับเด็กอายุต่ำกว่า 2 ปี)**

ความยาว (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)						เพศหญิง : น้ำหนัก (กิโลกรัม)					
	ผอม < - 2 S.D.	ค่อนข้างผอม ถึง <- 1.5 S.D.	ส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	ผอม <- 2 S.D.	ค่อนข้างผอม ถึง <- 1.5 S.D.	ส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.
80	9.1	9.2 - 9.5	9.6 - 11.9	12.0 - 12.4	12.5 - 13.2	13.3	8.5	8.6 - 8.9	9.0 - 11.2	11.3 - 11.6	11.7 - 12.3	12.4
81	9.3	9.4 - 9.7	9.8 - 12.2	12.3 - 12.6	12.7 - 13.5	13.6	8.7	8.8 - 9.1	9.2 - 11.4	11.5 - 11.8	11.9 - 12.6	12.7
82	9.5	9.6 - 9.9	10.0 - 12.5	12.6 - 12.9	13.0 - 13.8	13.9	8.8	8.9 - 9.2	9.3 - 11.7	11.8 - 12.0	12.1 - 12.8	12.9
83	9.8	9.9 - 10.1	10.2 - 12.7	12.8 - 13.2	13.3 - 14.1	14.2	9.0	9.1 - 9.4	9.5 - 11.9	12.0 - 12.3	12.4 - 13.0	13.1
84	10.0	10.1 - 10.3	10.4 - 13.0	13.1 - 13.5	13.6 - 14.5	14.6	9.2	9.3 - 9.6	9.7 - 12.1	12.2 - 12.5	12.6 - 13.3	13.4

ตารางที่ 4 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์สูง (สำหรับเด็กอายุ 2-18 ปี)													
ส่วนสูง (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)						เพศหญิง : น้ำหนัก (กิโลกรัม)						
	ผอม < - 2 S.D.	ค่อนข้างผอม ถึง < - 1.5 S.D.	ส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ทั่ว ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	ผอม < - 2 S.D. ถึง < - 1.5 S.D.	ค่อนข้างผอม ถึง < - 1.5 S.D.	ส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ทั่ว ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	
85	9.9	10.0 - 10.3	10.4 - 13.9	14.0 - 14.7	14.8 - 16.2	16.3	9.7	9.8 - 10.1	10.2 - 13.5	13.6 - 14.2	14.3 - 15.6	15.7	
86	10.1	10.2 - 10.5	10.6 - 14.1	14.2 - 14.9	15.0 - 16.4	16.5	9.9	10.0 - 10.3	10.4 - 13.8	13.9 - 14.5	14.6 - 15.9	16.0	
87	10.3	10.4 - 10.7	10.8 - 14.3	14.4 - 15.1	15.2 - 16.6	16.7	10.1	10.2 - 10.5	10.6 - 14.0	14.1 - 14.7	14.8 - 16.0	16.1	
88	10.5	10.6 - 10.9	11.0 - 14.6	14.7 - 15.4	15.5 - 16.9	17.0	10.3	10.4 - 10.7	10.8 - 14.3	14.4 - 15.0	15.1 - 16.4	16.5	
89	10.8	10.9 - 11.3	11.4 - 15.0	15.1 - 15.7	15.8 - 17.1	17.2	10.5	10.6 - 10.9	11.0 - 14.6	14.7 - 15.3	15.4 - 16.7	16.8	
90	11.0	11.1 - 11.5	11.6 - 15.2	15.3 - 15.9	16.0 - 17.3	17.4	10.7	10.8 - 11.2	11.3 - 14.8	14.9 - 15.5	15.6 - 16.8	16.9	
91	11.2	11.3 - 11.7	11.8 - 15.5	15.6 - 16.2	16.3 - 17.6	17.7	10.9	11.0 - 11.4	11.5 - 15.1	15.2 - 15.8	15.9 - 17.1	17.2	
92	11.4	11.5 - 11.9	12.0 - 15.8	15.9 - 16.5	16.6 - 17.9	18.0	11.1	11.2 - 11.6	11.7 - 15.4	15.5 - 16.1	16.2 - 17.5	17.6	
93	11.6	11.7 - 12.1	12.2 - 16.0	16.1 - 16.8	16.9 - 18.3	18.4	11.3	11.4 - 11.8	11.9 - 15.7	15.8 - 16.4	16.5 - 17.8	17.9	
94	11.9	12.0 - 12.4	12.5 - 16.4	16.5 - 17.2	17.3 - 18.7	18.8	11.5	11.6 - 12.0	12.1 - 16.0	16.1 - 16.7	16.8 - 18.1	18.2	

ตารางที่ 4 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์สูง (สำหรับเด็กอายุ 2-18 ปี)														
ส่วนสูง (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)							เพศหญิง : น้ำหนัก (กิโลกรัม)						
	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < - 1.5 S.D.	ส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < - 1.5 S.D.	ส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.		
95	12.1	12.2 - 12.6	12.7 - 16.7	16.8 - 17.5	17.6 - 19.1	19.2	11.7	11.8 - 12.2	12.3 - 16.2	16.3 - 17.0	17.1 - 18.5	18.6		
96	12.3	12.4 - 12.8	12.9 - 17.0	17.1 - 17.8	17.9 - 19.4	19.5	12.0	12.1 - 12.5	12.6 - 16.5	16.6 - 17.3	17.4 - 18.8	18.9		
97	12.5	12.6 - 13.0	13.1 - 17.3	17.4 - 18.1	18.2 - 19.7	19.8	12.2	12.3 - 12.7	12.8 - 16.9	17.0 - 17.7	17.8 - 19.2	19.3		
98	12.7	12.8 - 13.2	13.3 - 17.6	17.7 - 18.4	18.5 - 20.1	20.2	12.4	12.5 - 12.9	13.0 - 17.2	17.3 - 18.0	18.1 - 19.6	19.7		
99	13.0	13.1 - 13.5	13.6 - 17.9	18.0 - 18.7	18.8 - 20.4	20.5	12.6	12.7 - 13.2	13.3 - 17.6	17.7 - 18.4	18.5 - 20.0	20.1		
100	13.2	13.3 - 13.7	13.8 - 18.2	18.3 - 19.0	19.1 - 20.7	20.8	12.9	13.0 - 13.4	13.5 - 17.9	18.0 - 18.7	18.8 - 20.4	20.5		
101	13.4	13.5 - 13.9	14.0 - 18.4	18.5 - 19.3	19.4 - 21.1	21.2	13.1	13.2 - 13.7	13.8 - 18.2	18.3 - 19.1	19.2 - 20.9	21.0		
102	13.7	13.8 - 14.2	14.3 - 18.7	18.8 - 19.6	19.7 - 21.4	21.5	13.3	13.4 - 13.9	14.0 - 18.5	18.6 - 19.4	19.5 - 21.2	21.3		
103	13.9	14.0 - 14.5	14.6 - 19.0	19.1 - 19.9	20.0 - 21.7	21.8	13.4	13.5 - 14.1	14.2 - 18.9	19.0 - 19.8	19.9 - 21.7	21.8		
104	14.1	14.2 - 14.7	14.8 - 19.4	19.5 - 20.3	20.4 - 22.2	22.3	13.7	13.8 - 14.4	14.5 - 19.2	19.3 - 20.1	20.2 - 22.0	22.1		
105	14.4	14.5 - 15.0	15.1 - 19.7	19.8 - 20.6	20.7 - 22.5	22.6	13.9	14.0 - 14.6	14.7 - 19.6	19.7 - 20.5	20.6 - 22.4	22.5		
106	14.5	14.6 - 15.2	15.3 - 20.1	20.2 - 21.0	21.1 - 22.9	23.0	14.2	14.3 - 14.9	15.0 - 20.0	20.1 - 20.9	21.0 - 22.9	23.0		
107	14.8	14.9 - 15.5	15.6 - 20.5	20.6 - 21.4	21.5 - 23.4	23.5	14.4	14.5 - 15.1	15.2 - 20.3	20.4 - 21.3	21.4 - 23.4	23.5		
108	15.0	15.1 - 15.7	15.8 - 20.8	20.9 - 21.7	21.8 - 23.7	23.8	14.7	14.8 - 15.4	15.5 - 20.7	20.8 - 21.7	21.8 - 23.8	23.9		
109	15.3	15.4 - 16.0	16.1 - 21.1	21.2 - 22.1	22.2 - 24.2	24.3	14.9	15.0 - 15.6	15.7 - 21.1	21.2 - 22.2	22.3 - 24.3	24.4		

ตารางที่ 4 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์สูง (สำหรับเด็กอายุ 2-18 ปี)														
ส่วนสูง (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)							เพศหญิง : น้ำหนัก (กิโลกรัม)						
	ห่อม	ค่อนข้างห่อม	สมส่วน	ท้วม	เริ่มอ้วน	อ้วน	ห่อม	ค่อนข้างห่อม	สมส่วน	ท้วม	เริ่มอ้วน	อ้วน		
	< - 2 S.D. ถึง < - 1.5 S.D.	- 2 S.D. ถึง < - 1.5 S.D.	- 1.5 S.D. ถึง + 1.5 S.D.	> + 1.5 S.D. ถึง + 2 S.D.	> + 2 S.D. ถึง + 3 S.D.	> + 3 S.D.	< - 2 S.D. ถึง < - 1.5 S.D.	- 2 S.D. ถึง < - 1.5 S.D.	- 1.5 S.D. ถึง + 1.5 S.D.	> + 1.5 S.D. ถึง + 2 S.D.	> + 2 S.D. ถึง + 3 S.D.	> + 3 S.D.		
110	15.6	15.7 - 16.3	16.4 - 21.6	21.7 - 22.7	22.8 - 24.8	24.9	15.2	15.3 - 15.9	16.0 - 21.5	21.6 - 22.6	22.7 - 24.7	24.8		
111	15.9	16.0 - 16.6	16.7 - 22.0	22.1 - 23.1	23.2 - 25.2	25.3	15.4	15.5 - 16.2	16.3 - 21.9	22.0 - 23.1	23.2 - 25.4	25.5		
112	16.1	16.2 - 16.8	16.9 - 22.3	22.4 - 23.5	23.6 - 25.7	25.8	15.7	15.8 - 16.5	16.6 - 22.3	22.4 - 23.5	23.6 - 25.8	25.9		
113	16.4	16.5 - 17.1	17.2 - 22.8	22.9 - 24.0	24.1 - 26.3	26.4	16.0	16.1 - 16.8	16.9 - 22.8	22.9 - 24.0	24.1 - 26.4	26.5		
114	16.7	16.8 - 17.4	17.5 - 23.3	23.4 - 24.5	24.6 - 26.9	27.0	16.3	16.4 - 17.1	17.2 - 23.2	23.3 - 24.5	24.6 - 27.0	27.1		
115	17.0	17.1 - 17.8	17.9 - 23.8	23.9 - 25.0	25.1 - 27.4	27.5	16.6	16.7 - 17.4	17.5 - 23.7	23.8 - 25.0	25.1 - 27.6	27.7		
116	17.3	17.4 - 18.1	18.2 - 24.2	24.3 - 25.5	25.6 - 28.1	28.2	16.8	16.9 - 17.6	17.7 - 24.3	24.4 - 25.6	25.7 - 28.3	28.4		
117	17.6	17.7 - 18.4	18.5 - 24.8	24.9 - 26.1	26.2 - 28.8	28.9	17.1	17.2 - 17.9	18.0 - 24.7	24.8 - 26.1	26.2 - 28.9	29.0		
118	18.0	18.1 - 18.8	18.9 - 25.2	25.3 - 26.6	26.7 - 29.4	29.5	17.4	17.5 - 18.3	18.4 - 25.3	25.4 - 26.7	26.8 - 29.6	29.7		
119	18.3	18.4 - 19.1	19.2 - 25.8	25.9 - 27.2	27.3 - 30.1	30.2	17.7	17.8 - 18.6	18.7 - 25.8	25.9 - 27.4	27.5 - 30.4	30.5		
120	18.6	18.7 - 19.4	19.5 - 26.4	26.5 - 27.9	28.0 - 30.8	30.9	18.1	18.2 - 19.0	19.1 - 26.5	26.6 - 28.1	28.2 - 31.3	31.4		
121	18.9	19.0 - 19.7	19.8 - 26.9	27.0 - 28.5	28.6 - 31.6	31.7	18.4	18.5 - 19.3	19.4 - 27.1	27.2 - 28.7	28.8 - 31.9	32.0		
122	19.3	19.4 - 20.1	20.2 - 27.5	27.6 - 29.1	29.2 - 32.3	32.4	18.7	18.8 - 19.6	19.7 - 27.7	27.8 - 29.4	29.5 - 32.8	32.9		
123	19.6	19.7 - 20.4	20.5 - 28.0	28.1 - 29.7	29.8 - 33.0	33.1	19.0	19.1 - 19.9	20.0 - 28.4	28.5 - 30.2	30.3 - 33.8	33.9		
124	20.0	20.1 - 20.8	20.9 - 28.7	28.8 - 30.4	30.5 - 33.9	34.0	19.4	19.5 - 20.4	20.5 - 29.1	29.2 - 30.9	31.0 - 34.7	34.8		

ตารางที่ 4 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์ส่วนสูง (สำหรับเด็กอายุ 2-18 ปี)														
ส่วนสูง (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)							เพศหญิง : น้ำหนัก (กิโลกรัม)						
	ผอม < -2 S.D.	ค่อนข้างผอม -2 S.D. ถึง <-1.5 S.D.	สมส่วน -1.5 S.D. ถึง +1.5 S.D.	ท้วม > +1.5 S.D. ถึง +2 S.D.	เริ่มอ้วน > +2 S.D. ถึง +3 S.D.	อ้วน > +3 S.D.	ผอม < -2 S.D.	ค่อนข้างผอม -2 S.D. ถึง <-1.5 S.D.	สมส่วน -1.5 S.D. ถึง +1.5 S.D.	ท้วม > +1.5 S.D. ถึง +2 S.D.	เริ่มอ้วน > +2 S.D. ถึง +3 S.D.	อ้วน > +3 S.D.		
125	20.3	20.4 - 21.2	21.3 - 29.3	29.4 - 31.0	31.1 - 34.5	34.6	19.7	19.8 - 20.7	20.8 - 29.8	29.9 - 31.8	31.9 - 35.7	35.8		
126	20.7	20.8 - 21.6	21.7 - 29.9	30.0 - 31.7	31.8 - 35.3	35.4	19.9	20.0 - 21.0	21.1 - 30.5	30.6 - 32.6	32.7 - 36.7	36.8		
127	21.1	21.2 - 22.0	22.1 - 30.7	30.8 - 32.6	32.7 - 36.3	36.4	20.3	20.4 - 21.5	21.6 - 31.3	31.4 - 33.4	33.5 - 37.7	37.8		
128	21.4	21.5 - 22.4	22.5 - 31.3	31.4 - 33.3	33.4 - 37.1	37.2	20.6	20.7 - 21.8	21.9 - 32.0	32.1 - 34.2	34.3 - 38.6	38.7		
129	21.8	21.9 - 22.8	22.9 - 32.1	32.2 - 34.1	34.2 - 38.1	38.2	21.0	21.1 - 22.2	22.3 - 32.8	32.9 - 35.2	35.3 - 39.8	39.9		
130	22.1	22.2 - 23.2	23.3 - 32.9	33.0 - 35.0	35.1 - 39.2	39.3	21.3	21.4 - 22.6	22.7 - 33.7	33.8 - 36.1	36.2 - 40.9	41.0		
131	22.5	22.6 - 23.7	23.8 - 33.7	33.8 - 35.9	36.0 - 40.3	40.4	21.7	21.8 - 23.0	23.1 - 34.5	34.6 - 37.0	37.1 - 42.0	42.1		
132	23.0	23.1 - 24.2	24.3 - 34.6	34.7 - 36.8	36.9 - 41.4	41.5	22.1	22.2 - 23.4	23.5 - 35.3	35.4 - 37.9	38.0 - 43.1	43.2		
133	23.4	23.5 - 24.6	24.7 - 35.4	35.5 - 37.8	37.9 - 42.5	42.6	22.5	22.6 - 23.9	24.0 - 36.2	36.3 - 38.8	38.9 - 44.2	44.3		
134	23.8	23.9 - 25.1	25.2 - 36.2	36.3 - 38.7	38.8 - 43.6	43.7	22.9	23.0 - 24.3	24.4 - 37.1	37.2 - 39.9	40.0 - 45.4	45.5		
135	24.3	24.4 - 25.6	25.7 - 37.1	37.2 - 39.6	39.7 - 44.7	44.8	23.2	23.3 - 24.8	24.9 - 38.0	38.1 - 40.8	40.9 - 46.4	46.5		
136	24.7	24.8 - 26.0	26.1 - 37.9	38.0 - 40.5	40.6 - 45.7	45.8	23.7	23.8 - 25.3	25.4 - 38.9	39.0 - 41.8	41.9 - 47.6	47.7		
137	25.2	25.3 - 26.5	26.6 - 38.8	38.9 - 41.4	41.5 - 46.8	46.9	24.1	24.2 - 25.8	25.9 - 39.8	39.9 - 42.7	42.8 - 48.6	48.7		
138	25.6	25.7 - 27.0	27.1 - 39.6	39.7 - 42.4	42.5 - 47.8	47.9	24.6	24.7 - 26.3	26.4 - 40.6	40.7 - 43.6	43.7 - 49.6	49.7		
139	26.1	26.2 - 27.5	27.6 - 40.4	40.5 - 43.2	43.3 - 48.7	48.8	25.1	25.2 - 26.9	27.0 - 41.6	41.7 - 44.6	44.7 - 50.7	50.8		

ตารางที่ 4 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์สูง (สำหรับเด็กอายุ 2-18 ปี)														
ส่วนสูง (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)							เพศหญิง : น้ำหนัก (กิโลกรัม)						
	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < -1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < -1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.		
140	26.5	26.6 - 28.1	28.2 - 41.2	41.3 - 44.1	44.2 - 49.8	49.9	25.7	25.8 - 27.5	27.6 - 42.4	42.5 - 45.5	45.6 - 51.8	51.9		
141	27.0	27.1 - 28.6	28.7 - 42.0	42.1 - 44.9	45.0 - 50.7	50.8	26.1	26.2 - 28.1	28.2 - 43.4	43.5 - 46.6	46.7 - 52.9	53.0		
142	27.5	27.6 - 29.1	29.2 - 42.8	42.9 - 45.7	45.8 - 51.5	51.6	26.7	26.8 - 28.7	28.8 - 44.3	44.4 - 47.5	47.6 - 53.8	53.9		
143	28.0	28.1 - 29.6	29.7 - 43.5	43.6 - 46.5	46.6 - 52.5	52.6	27.3	27.4 - 29.4	29.5 - 45.2	45.3 - 48.4	48.5 - 54.7	54.8		
144	28.5	28.6 - 30.2	30.3 - 44.3	44.4 - 47.3	47.4 - 53.4	53.5	28.0	28.1 - 30.1	30.2 - 46.1	46.2 - 49.3	49.4 - 55.7	55.8		
145	29.1	29.2 - 30.8	30.9 - 45.2	45.3 - 48.2	48.3 - 54.4	54.5	28.6	28.7 - 30.7	30.8 - 47.0	47.1 - 50.3	50.4 - 56.8	56.9		
146	29.6	29.7 - 31.3	31.4 - 45.9	46.0 - 49.0	49.1 - 55.3	55.4	29.3	29.4 - 31.5	31.6 - 47.9	48.0 - 51.2	51.3 - 57.7	57.8		
147	30.2	30.3 - 31.9	32.0 - 46.7	46.8 - 49.9	50.0 - 56.2	56.3	30.1	30.2 - 32.3	32.4 - 48.8	48.9 - 52.1	52.2 - 58.6	58.7		
148	30.8	30.9 - 32.5	32.6 - 47.6	47.7 - 50.8	50.9 - 57.2	57.3	30.8	30.9 - 33.0	33.1 - 49.7	49.8 - 53.0	53.1 - 59.5	59.6		
149	31.4	31.5 - 33.2	33.3 - 48.4	48.5 - 51.6	51.7 - 58.0	58.1	31.4	31.5 - 33.8	33.9 - 50.5	50.6 - 53.8	53.9 - 60.3	60.4		
150	32.0	32.1 - 33.8	33.9 - 49.1	49.2 - 52.4	52.5 - 58.9	59.0	32.2	32.3 - 34.5	34.7 - 51.4	51.5 - 54.7	54.8 - 61.2	61.3		
151	32.7	32.8 - 34.5	34.6 - 49.9	50.0 - 53.2	53.3 - 59.7	59.8	33.0	33.1 - 35.4	35.5 - 52.2	52.3 - 55.5	55.6 - 62.0	62.1		
152	33.2	33.3 - 35.1	35.2 - 50.7	50.8 - 54.0	54.1 - 60.5	60.6	33.7	33.8 - 36.1	36.2 - 53.0	53.1 - 56.3	56.4 - 62.8	62.9		
153	33.9	34.0 - 35.9	36.0 - 51.5	51.6 - 54.8	54.9 - 61.3	61.4	34.5	34.6 - 36.9	37.0 - 53.8	53.9 - 57.1	57.2 - 63.6	63.7		
154	34.5	34.6 - 36.5	36.6 - 52.3	52.4 - 55.6	55.7 - 62.1	62.2	35.2	35.3 - 37.6	37.7 - 54.6	54.7 - 57.9	58.0 - 64.4	64.5		

ตารางที่ 4 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์ส่วนสูง (สำหรับเด็กอายุ 2-18 ปี)														
ส่วนสูง (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)							เพศหญิง : น้ำหนัก (กิโลกรัม)						
	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < - 1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < - 1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.		
155	35.2	35.3 - 37.2	37.3 - 53.1	53.2 - 56.4	56.5 - 62.9	63.0	35.9	36.0 - 38.3	38.4 - 55.4	55.5 - 58.7	58.8 - 65.2	65.3		
156	35.9	36.0 - 38.0	38.1 - 54.0	54.1 - 57.2	57.3 - 63.6	63.7	36.6	36.7 - 39.1	39.2 - 56.2	56.3 - 59.4	59.5 - 65.8	65.9		
157	36.6	36.7 - 38.7	38.8 - 54.8	54.9 - 58.0	58.1 - 64.3	64.4	37.3	37.4 - 39.8	39.9 - 56.9	57.0 - 60.1	60.2 - 66.4	66.5		
158	37.3	37.4 - 39.5	39.6 - 55.6	55.7 - 58.8	58.9 - 65.1	65.2	38.0	38.1 - 40.5	40.6 - 57.6	57.7 - 60.8	60.9 - 67.1	67.2		
159	38.0	38.1 - 40.2	40.3 - 56.5	56.6 - 59.7	59.8 - 66.0	66.1	38.7	38.8 - 41.2	41.3 - 58.3	58.4 - 61.4	61.5 - 67.7	67.8		
160	38.6	38.7 - 41.0	41.1 - 57.3	57.4 - 60.4	60.5 - 66.7	66.8	39.4	39.5 - 41.9	42.0 - 59.0	59.1 - 62.1	62.2 - 68.4	68.5		
161	39.4	39.5 - 41.8	41.9 - 58.2	58.3 - 61.2	61.3 - 67.4	67.5	40.0	40.1 - 42.6	42.7 - 59.7	59.8 - 62.7	62.8 - 68.8	68.9		
162	40.1	40.2 - 42.5	42.6 - 59.0	59.1 - 62.0	62.1 - 68.1	68.2	40.7	40.8 - 43.3	43.4 - 60.3	60.4 - 63.3	63.4 - 69.3	69.4		
163	40.8	40.9 - 43.3	43.4 - 59.8	59.9 - 62.8	62.9 - 68.8	68.9	41.4	41.5 - 44.1	44.2 - 61.1	61.2 - 64.0	64.1 - 69.8	69.9		
164	41.5	41.6 - 44.0	44.1 - 60.6	60.7 - 63.6	63.7 - 69.6	69.7	42.0	42.1 - 44.8	44.9 - 61.7	61.8 - 64.6	64.7 - 70.3	70.4		
165	42.2	42.3 - 44.8	44.9 - 61.5	61.6 - 64.4	64.5 - 70.2	70.3	42.7	42.8 - 46.5	45.6 - 62.3	62.4 - 65.1	65.2 - 70.6	70.7		
166	43.0	43.1 - 45.6	45.7 - 62.3	62.4 - 65.2	65.3 - 71.0	71.1	43.5	43.6 - 46.3	46.4 - 63.0	63.1 - 65.6	65.7 - 71.0	71.1		
167	43.7	43.8 - 46.3	46.4 - 63.1	63.2 - 66.0	66.1 - 71.7	71.8	44.2	44.3 - 47.1	47.2 - 63.6	63.7 - 66.2	66.3 - 71.4	71.5		
168	44.4	44.5 - 47.1	47.2 - 63.9	64.0 - 66.8	66.9 - 72.5	72.6	45.0	45.1 - 47.9	48.0 - 64.2	64.3 - 66.7	66.8 - 71.6	71.7		
169	45.0	45.1 - 47.8	47.9 - 64.7	64.8 - 67.5	67.7 - 73.3	73.4	45.8	45.9 - 48.7	48.8 - 64.9	65.0 - 67.3	67.4 - 72.1	72.2		

ตารางที่ 4 แสดงเกณฑ์อ้างอิงการเจริญเติบโตน้ำหนักตามเกณฑ์ส่วนสูง (สำหรับเด็กอายุ 2-18 ปี)												
ส่วนสูง (ซม.)	เพศชาย : น้ำหนัก (กิโลกรัม)						เพศหญิง : น้ำหนัก (กิโลกรัม)					
	ผอม < - 2 S.D.	ค่อนข้างผอม - 2 S.D. ถึง < -1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.	ผอม < - 2 S.D.	ค่อนข้างผอม ถึง < - 1.5 S.D.	สมส่วน - 1.5 S.D. ถึง + 1.5 S.D.	ท้วม > + 1.5 S.D. ถึง + 2 S.D.	เริ่มอ้วน > + 2 S.D. ถึง + 3 S.D.	อ้วน > + 3 S.D.
170	45.7	46.8 - 48.5	48.5 - 55.5	55.6 - 65.3	68.4 - 73.8	73.9	46.7	46.8 - 49.7	49.8 - 65.5	65.6 - 67.7	67.8 - 72.3	72.4
171	46.4	46.5 - 49.3	49.4 - 66.3	66.4 - 69.1	69.2 - 74.6	74.7						
172	47.1	47.2 - 50.0	50.1 - 67.0	67.1 - 69.8	69.9 - 75.3	75.4						
173	47.9	48.0 - 50.8	50.9 - 67.7	67.8 - 70.5	70.6 - 75.9	76.0						
174	48.6	48.7 - 51.5	51.6 - 68.5	68.6 - 71.1	71.2 - 76.5	76.6						
175	49.4	49.5 - 52.3	52.4 - 69.2	69.3 - 71.8	71.9 - 77.2	77.3						
176	50.1	50.2 - 53.0	53.1 - 69.9	70.0 - 72.5	72.6 - 77.9	78.0						
177	50.9	51.0 - 53.8	53.9 - 70.6	70.7 - 73.2	73.3 - 78.6	78.7						
178	51.7	51.8 - 54.6	54.7 - 71.2	71.3 - 73.8	73.9 - 79.1	79.2						
179	52.5	52.6 - 55.4	55.5 - 71.9	72.0 - 74.5	74.6 - 79.8	79.9						
180	53.3	53.4 - 56.1	56.2 - 72.4	72.5 - 75.0	75.1 - 80.2	80.3						

## **BIOGRAPHY**

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