RECOMMENDATION STRATEGIES FOR THE PREVENTION AND CONTROL OF HIGH MORBIDITY OF DENGUE HEMORRHAGIC FEVER IN NORTH SUMATERA PROVINCE

FAZIDAH AGUSLINA SIREGAR

UNIVERSITI SAINS MALAYSIA

2016

RECOMMENDATION STRATEGIES FOR THE PREVENTION AND CONTROL OF HIGH MORBIDITY OF DENGUE HEMORRHAGIC FEVER IN NORTH SUMATERA PROVINCE

by

FAZIDAH AGUSLINA SIREGAR

Thesis submitted in fulfillment of the requirements
for the degrees of
Doctor of Philosophy

March 2016

ACKNOWLEDGEMENT

First and foremost, I wish to extend my greatest gratitude and many thanks to my supervisors, Prof. Dr. Mohamed Rusli Abdullah MD, MPH, PhD, co supervisor Prof. Dr. Sori Muda Sarumpaet.MPH and Teguh Supriyadi, SKM.MPH for their helpful guidance and support to carry out this study and to complete this disertation. I am also very grateful to Prof Dr Ahmad Sukari Halim, Dean of School of Medical Science, University Sains Malaysia, for giving me the opportunity to complete my study.

I am sincerely very grateful to Head of North Sumatera University Prof. Dr. Runtung Sitepu, SH., M.Hum for giving me the opportunity to attend and facilitate to complete the PhD programme at the School of Medical Science, University Sains Malaysia. I am also grateful to Dean of Public Health Faculty of North Sumatera University DR.Drs Surya Utama, MS for giving me support to complete my study

Thank you also to all those involved in this study namely, all the staff of Hospital, Health Facility and Health District Office in the place of study in North Sumatera Province, data collector and patients and community who used their time to participate in this study, I am sincerely grateful.

Last but not least, thank you to my parents, parents in law, my husband, Dr Tri Makmur SpS and my children, Muhammmad Arbuya Agustrifa, Muhammad Armiza Trifamar and Armadina Trifamar for their love and care throughout the whole journey.

TABLE OF CONTENTS

Acknowledgments ii

Table of Content iv

List of Tables ……..... xii

List of Figures..... xxii

List of Abbreviations xli

Abstrak ……..... xliii

Abstract ……. xlvi

CHAPTER 1. INTRODUCTION

1.1 Background …….. 1

1.2 Problem statements…… 8

1.3 Rationale of the study …….. 10

1.4 Objectives of study …….. 11

1.4.1. General objective…….. 11

1.4.2. Specific objective……..... 11

1.5. Hypothesis …….. 11

1.6. Conceptual framework …… 13

CHAPTER 2. LITERATURE REVIEW.

2.1. The epidemiology of dengue fever and dengue hemorrhagic fever….. 14

2.1.1 Dengue fever and dengue hemorrhagic fever…..…….. 14

2.1.2 Etiology of dengue infection ……. 16

2.1.3 Transmission…… 18

2.1.4 Epidemiology of dengue hemorrhagic fever…….. 22

2.1.5 Factors associated with dengue hemorrhagic fever …… 23

2.1.6 Pathogenesis…… 32

2.1.7 Clinical manifestation …….. 35

2.1.8 Diagnosis of dengue hemorrhagic fever…… 36

2.1.9 Dengue prevention and control…….. 38

2.2 The global phenomena of dengue hemorrhagic fever …….. 38

2.3 Impact of dengue hemorrhagic fever…… 40

2.4 Surveillance for dengue hemorrhagic fever ……..... 42

2.4.1 Definition of surveillance…….. 42

2.4.2 Approach of surveillance system for dengue hemorrhagic fever 44

2.4.3 Uses of surveillance for dengue hemorrhagic fever……. 47

2.4.4 Evaluation of surveillance system …… 48

2.4.5 Management of surveillance system……. 49

2.4.6 Effective surveillance system for dengue hemorrhagic fever… 50

CHAPTER 3. GENERAL OVERVIEW OF THE STUDY

3.1 Study areas …….. 54

3.1.1 Description of the study areas ……. 54

3.1.1.1 North Sumatera Province …….. 54

3.1.1.2 The selected districts in study area …… 56

3.2 Study component ……. 62

3.3 Methodology of the study …… 63

CHAPTER 4. EXPLORATORY STUDY

4.1 Introduction…… 64

4.2 Materials and methods…….. 65

4.2.1 Study design…… 65

4.2.2 Sampling methods and sample size determination……. 66

4.2.2.1 Sampling methods …… 66

4.2.2.2 Sample size determination…… 70

4.2.3 Data collection : tools and instruments……. 71

4.2.3.1 Development of questionnaires and proforma …… 71

4.2.3.2 Validation of questionnaires ……. 73

4.2.4 Data entry and analysis……. 74

4.3 Results…… 74

4.3.1 Management and policy of the Surveillance System……. 74

4.3.2 Validation of questionnaire …….. 76

4.3.3 Surveillance system at the health facility level ……..... 76

4.3.4 Surveillance system at the district health level…….. 88

4.3.4.1 Surveillance staff at the district health level ……. 89

4.3.4.2 Section head of surveillance system…… 99

4.3.4.3 Division head of surveillance system…… 102

4.4 Discussion …… 104

CHAPTER 5. CASE COHORT STUDY

5.1 Introduction…….. …… 120

5.2. Materials and methods……. 122

5.2.1 Study design……. 122

5.2.2 Case definition and case ascertainment …… 123

5.2.2.1 Defintion and case ascertainment …… 123

5.2.2.2 Definition and ascertainment of subcohort……. 124

5.2.2.3 Definition of caregivers ……. 125

5.2.2.4. Test procedure……. 125

5.2.2.4(a)Procedure for detection of IgG /IgM …… 125

5.2.2.4(b)Correlation / verification of whole blood vs finger prick……. 127

5.2.3 Sampling methods and sample size determination…… 128

5.2.3.1 Sampling methods…… 128

5.2.3.2 Sample size determination…… 129

5.2.4 Data collection: tools and instruments …….. 131

5.2.4.1 Socio-demographic factors……. 131

5.2.4.2 Knowledge attitude practice…… 132

5.2.4.3 Environmental factors…….. 133

5.2.5 Validation of questionnaires……. 134

5.2.6 Data entry and analysis…… 135

5.3 Result …….. 136

5.3.1 Test and laboratory procedures…….. 136

5.3.1.1 Sensitivity and specificity…….. 136

5.3.1.2 Correlation of whole blood and finger prick …… 137

5.3.1.3 Validation of questionnaires…….. 139

5.3.2 Socio-demographic data…….. 147

5.3.2.1 Socio-demographic of the samples …… 147

5.3.2.2 Socio-demographic of characteristics of caregivers .. 147

5.3.3 Socioculture of the caregivers……. 149

5.3.4 Knowledge attitude and practice of the caregivers …… 151

5.3.5 House characteristic and its environment……. 151

5.3.6 Factors among cases, sub-cohort and caregivers associated with dengue hemorrhagic fever in North Sumatera Province ……. 153

5.3.6.1 Factors among cases and sub-cohort associated with dengue hemorrhagic fever ……. 153

5.3.6.2 Factors among caregivers in cases and sub-cohort associated with dengue hemorrhagic fever …… 161

5.4 Discussion …… 171

CHAPTER 6. COMPARATIVE CROSSSECTIONAL STUDY

6.1 Introduction…….. 182

6.2 Materials and methods…….. 184

6.2.1 Study design ……. 184

6.2.2 Sampling methods and sample size determination ……..... 184

6.2.2.2 Sampling methods …… 184

6.2.2.3 Sample size determination ……. 189

6.2.3 Data collection: tools and instruments……. 193

6.2.4 Data entry and analysis……. 193

6.3 Result…….. 193

6.3.1 Validation of questionnaires……. 193

6.3.2 Socio-demographic data of respondents……. 194

6.3.3 Socio-culture profile of respondents…… 195

6.3.4 Knowledge attitudes and practices of respondents……. 197

6.3.5 House characteristics and its environment…….. 197

6.3.6 Factors associated with dengue hemorrhagic fever in high Incidence district In North Sumatera Province ……. 199

6.4 Discussion ……. 208

CHAPTER 7. ENTOMOLOGY STUDY

7.1 Introduction……. 218

7.2 Materials and methods…… 219

7.2.1 Study design…… 219

7.2.2 Sampling methods and sample size determination ……. 220

7.2.2.1. Sampling methods…… 220

7.2.2.2 Sample size determination…….. 223

7.2.3 Data collection : tools and instruments…… 225

7.2.3.1 Questionnaire and proforma …… 225

7.2.3.2 Larval survey…….. 226

7.2.3.3 Adult mosquitoes survey…….…… 229

7.2.4 Indices of Aedes density……. 231

7.2.4 (a) Larval indices……. . 231

7.2.4 (b) Adult indices…….. 232

7.2.5 Data entry and analysis…….. 233

7.3. Result……. 233

7.3.1 Socio-cultural and environmental factors associated with dengue hemorrhagic fever transmission in North Sumatera Sumatera Province ……. 233

7.3.2 Larval and mosquitoes survey…….. 237

7.3.2.1 Type of containers indoor and outdoor houses …… 237

7.3.3.2 Larval and adult indices…… 240

7.3.3. Distribution pattern of Aedes larvae and adult mosquitoes …… 244

7.4 Discussion……. 251

CHAPTER 8. CLIMATIC STUDY

8.1 Introduction…….. 264

8.2 Materials and methods…… 266

8.2.1 Study Area ……. 266

8.2.2 Study design……..... 266

8.2.3 Sampling methods and sample size determination……. 267

8.2.4 Data collection : tools and instruments…… 270

8.2.5 Data entry and analysis…….

270

8.3 Result…….. 271

8.3.1 Medan district……..…….. 271

8.3.2 Pematang Siantar district ……. 284

8.3.3 Tebing Tinggi district …….. 296

8.3.4 Langkat district …… 307

8.3.5 Asahan district ……. 319

8.3.6 Deli Serdang district …… 330

8.4. Discussion …….. 342

CHAPTER 9. CONCLUSION AND RECOMMENDATION..... 347

9.1 Conclusion ……. 347

9.2.Recommendation……. 348

REFERENCES…… 350

APPENDICES .....

Appendix 1.Ethical approval letter from North Sumatera University…… 376

Appendix 2. Letter of study permit ……. 377

Appendix 3 Form of notice of study…….. 379

Appendix 4 Form of inform consent ……. 381

Appendix 5 Questionnaire…….. 383

Appendix 6 Climate data and DHF data…… 431

Appendix 7 Publication ……. 453

LIST OF TABLES

Table 2.1 Grading of dengue hemorrhagic fever according to WHO…. 15

Table 3.1 Sociodemographic and geography of district with high and Low DHF incidence in North Sumatera Province…… 60

Table 4.1 Staffing for dengue surveillance……. 71

Table 4.2 Questionnaire for health personnel in surveillance task at the health facility and district health office……. 72

Tabel 4.3 Reliability test of questionnaire in the exploratory study …… 76

Table 4.4 Sociodemography of surveillance staff at the health facility in North Sumatra Province…… 77

Table 4.5 Job description of surveillance staff at the health facility in North Sumatera Province……. 78

Table 4.6 Basic requirements in the implementation of a surveillance system at the health facility in North Sumatera Province…… 80

Table 4.7 Involvement of surveillance staff in the process of surveillance system in the health facility in North Sumatera Province …… 81

Table 4.8 Satisfaction survey among surveillance staff at the health facility of North Sumatera Province on dengue hemorrhagic fever surveillance system……. 87

Table 4.9 Motivation to carry out the surveillance system and an opinion toward an importance of survelance system among surveillance staff at health facility fn North Sumatera Province…….. 88

Table 4.10 Sociodemography of respondents in the district health level in North Sumatera Province…….. 89

Table 4.11 Job Description of respondents at the district health level in North Sumatera Province…… 90

Table 4.12 Basic requirements in the implementation of a surveillance system at the district health level in North Sumatera Province 91

Table 4.13 Involvement of surveillance staff in the process and attribute of surveillance system in district health level of North Sumatera Province…….. 92

Table 4.14 Satisfaction survey among surveillance staff in district health office of North Sumatera Province on dengue hemorrhagic fever surveillance system…….. 98

Table 4.15 Motivation to carry out the surveillance system and an opinion Toward in surveillance tasks among surveillance staff at the district health facilities in North Sumatera province…… 99

Table 4.16 Result of interview with the section head of surveillance system at the district health level …… 100

Table 4.17 Result of interview with the division head of surveillance system at the district health level …… 102

Table 5.1 Sensitivity test of Panbio Dengue Duo Cassette……. 136

Table 5.2 The Immunology Test IgG/IgM serology compared with whole blood…… 138

Table 5.3 Sensitivity and spesificity test from immunology test IgG/IgM using whole blood and serology from 29 dengue hemorrhagic fever cases……. 139

Table 5.4 The total variance table of knowledge question…… 141

Table 5.5 The distribution of rotation of loading factor for knowledge ….. 142

Table 5.6 Validity test for item of questions for knowledge…… 142

Table 5.7 Reliability test for item of questions for knowledge …… 143

Table 5.8 Kaiser Meyer Olkin and Bartlett's test for attitude ……. 144

Table 5.9 The total variance table of attitude question …… 144

Table 5.10 The distribution of rotation of loading factor for attitude…….. 145

Table 5.11 Validity test for item of questions for attitude…… 146

Tabl3 5.12 Reliability test for item of questions for attitude…… 146

Table 5.13 Socio-demography characteristics of the caregivers…… 148

Table 5.14 Sociocultural of the caregivers …… 150

Table 5.15 Knowledge attitudes and practices of the caregivers ……. 151

Table 5.16 House characteristics and its environment……. 152

Table 5.17 Factors among cases and sub- cohort associated with dengue hemorrhagic fever in North Sumatera Province by Simple Logistic Regression…….. 154

Table 5.18 Factors among cases and sub-cohort associated with the incidence of dengue hemorrhagic fever in North Sumatera Province by Multiple Logistic Regression …….. 157

Table 5.19 Output of multicollinearity……... 158

Table 5.20 Output of interaction…… 158

Table 5.21 Output of Hosmer lemeshow test …….. 159

Table 5.22 Output of classification table …….. 159

Table 5.23 Output of area under the ROC curve…….. 159

Table 5.24 Factors among cases and sub-cohort associated with dengue hemorrhagic fever in North Sumatera Province by Multiple Logistic Regression ……. 160

Table 5.25 Factors among caregivers in cases and sub-cohort associated with the dengue hemorrhagic fever in North Sumatera Province by Simple Logistic Regression …….. 162

Table 5.26 Factors among caregivers in cases and sub-cohort associated with the dengue hemorrhagic fever in North Sumatera Province by Multiple Logistic Regression …….. 166

Table 5.27 Output of multicollinearity …… 167

Table 5.28 Output of interaction…… 167

Table 5.29 Output of Hosmer lemeshow test …… 168

Table 5.30 Output of classification table …….. 168

Table 5.31 Output of area under the ROC curve……. 168

Table 5.32 Factors among caregivers in cases and sub-cohort associated with the dengue hemorrhagic fever in North Sumatera Province by Multiple Logistic Regression …….. 170

Table 6.1 Number of samples and sampling techniques in Comparative Study…….. 192

Table 6.2 Socio-demography characteristics of the respondents…….. 194

Table 6.3 Sociocultural profile of the respondents…… 196

Table 6.4 Knowledge, attitudes and practices of the respondents …….. 197

Table 6.5 House characteristics and its environment……. 198

Table 6.6 Factors associated with dengue hemorrhagic fever in high Incidence district in North Sumatera Province by Simple Logistic Regression……. 200

Table 6.7. Factors associated with the dengue hemorrhagic fever in high incidence district in North Sumatera by Multiple Logistic Regression……. 203

Table 6.8 Output of multicolinearity…… 204

Table 6.9 Output of Hosmer lemeshow test …… 204

Table 6.10 Output of classification table …… 205

Table 6.11 Output of area under the ROC Curve…….. 205

Table 6.12 Factors associated with dengue hemorrhagic fever in high incidence district in North Sumatera Province by Multiple Logistic Regression……. 207

Table 7.1 Socio-cultural and environmental factors associated with dengue hemorrhagic fever transmission n North Sumatera Province by Simple Logistic Regression…..... 234

Table 7.2 Socio-cultural and environmental factors associated with dengue hemorrhagic fever transmission n North Sumatera Province by Simple Logistic Regression ……..….. 236

Table 7.3 Type of containers and positive containers for Aedes larvae both indoor and outdoor house in high and low incidence district…… 238

Table 7.4 Effect of the number of container and positive container per houses on dengue hemorrhagic fever transmission in North Sumatera Province by Independent t test ……. 239

Table 7.5 Effect of the number of container and positive container per houses on dengue hemorrhagic fever transmission in North Sumatera Province by Two way Anova …….. 240

Table 7.6 Aedes larvae indices in the district with high and low dengue hemorrhagic fever in North Sumatera Province …… 241

Table 7.7 Aedes mosquitoe indices in the district with high and low dengue hemorrhagic fever in North Sumatera Province …..……. 243

Table 7.8 Correlation between larvae indices and adult indices in HIDs and LIDs in North Sumatera Province by Simple Logistic Regression …….. 244

Table7.9. Association between vector indices and dengue hemorrhagic fever transmission in North Sumatera Province by Simple Logistic Regression …….. 249

Table7.10. Association between vector indices and dengue hemorrhagic fever transmission in North Sumatera Province by Multiple Logistic Regression …….. 250

Table 8.1 The climatic factors and number of dengue Hemorrhagic fever cases in Medan district from 2003 to 2011 ……..... 271

Table 8.2 Correlation between climatic factors and number of dengue hemorrhagic fever cases in Medan district at the lag 0-3 months.. 274

Table 8.3 Cross correlation between climatic factors and number of dengue hemorrhagic fever cases in Medan district …….. 275

Table 8.4 Coefficient, standard error, t statistic and p value of parameters of SARIMA $(0,1,1)(0,1,1)_{12}$…….. 276

Table 8.5 Characteristic of Seasonal Autoregressive Integrated Moving Average models for dengue hemorrhagic fever and climatic variables in Medan district …….. 283

Table 8.6 Regression coefficient of climatic data on monthly dengue hemorrhagic fever in Medan district……. 284

Table 8.7 The climatic factors and number of dengue hemorrhagic fever cases in Pematang Siantar district from 2003 to 2011 …….. 285

Table 8.8.Correlation between climatic factors and dengue hemorrhagic fever cases in Pematang Siantar district at the lag 0-3 months..... 287

Table 8.9 Cross correlation between climatic factors and number of dengue hemorrhagic fever cases in Pematang Siantar district …….. 288

Table 8.10 Coefficient, standard error, t statistic and p value of parameters of SARIMA $(0,1,1)(0,1,1)_{12}$..... 289

Table 8.11 Characteristic of Seasonal Autoregressive Integrated Moving Avarage models for dengue hemorrhagic fever and climatic variable in Pematang Siantar district …… 295

Table 8.12 Regression coefficient of climatic data on monthly dengue hemorrhagic fever in Pematang Siantar district……. 296

Table 8.13 The climatic factors and number of dengue hemorrhagic fever cases in Tebing Tinggi district from 2003 to 2011 …….. 297

Table 8.14.Correlation between climatic factors and number of dengue hemorrhagic fever cases in Tebing Tinggi district at the lag of 0-3 months……. 299

Table 8.15 Cross correlation between climatic factors and number of dengue hemorrhagic fever cases in Tebing Tinggi district ……. 300

Table 8.16 Coefficient standard error, t statistic and p value of parameters of SARIMA $(0,1,1)(0,1,1)_{12}$..... 301

Table 8.17 Characteristic of Seasonal Autoregressive Integrated Moving Average models for dengue hemorrhagic fever and climatic variables in Tebing Tinggi district …… 307

Table 8.18 Regression coefficient of climatic data on monthly dengue hemorrhagic fever in Tebing Tinggi district …… 307

Table 8.19 The climatic factors and number of dengue hemorrhagic fever cases in Langkat district from 2003 to 2011 …….. 308

Table 8.20.Correlation between climatic factors and number of dengue hemorrhagic fever cases in Langkat district at the lag 0-3 months . …… 311

Table 8.21 Cross correlation between climatic factors and number of dengue hemorrhagic fever cases in Langkat district …..…. 311

Table 8.22 Coefficient standard error, t statistic and p value of parameters of SARIMA $(1,0,0)(1,1,0)_{12}$..... 312

Table 8.23 Characteristic of Seasonal Autoregressive Integrated Moving Average models for dengue hemorrhagic fever and climatic variables in Langkat district …… 318

Table8.24 Regression coefficient of climatic data on monthly number of dengue hemorrhagic fever in Langkat district……. 319

Table 8.25 The climatic factors and number of dengue hemorrhagic fever cases in Asahan district from 2003 to 2011 …… 320

Table 8.26.Correlation between climatic factors and number of dengue hemorrhagic fever cases in Asahan district at the lag 0-3 months..... 322

Table 8.27 Cross correlation between climatic factors and number of dengue hemorrhagic fever cases in Asahan district …… 323

Table 8.28 Coefficient, standard error, t statistic and p value of parameters of SARIMA $(0,1,1)(0,1,1)_{12}$…… 324

Table 8.29 Characteristic of Seasonal Autoregressive Integrated Moving Average models for dengue hemorrhagic fever and climatic variables in Asahan district ……. 330

Table 8.30 Regression coefficient of climatic data on monthly number of dengue hemorrhagic fever in Asahan district…….. 330

Table 8.31 The Climatic factors and number of dengue hemorrhagic fever cases in Deli Serdang district from 2003 to 2011 ……. 331

Table 8.32.Correlation between climatic factors and number of dengue hemorrhagic fever cases in Deli serdang district at the lag 0-3 months ….……. 334

Table 8.33 Cross correlation between climatic factors and number of dengue hemorrhagic fever cases in Deli Serdang district …. 334

Table 8.34 Coefficient standard error, t statistic and p value of parameters of SARIMA $(0,1,1)(0,1,1)_{12}$…… 335

Table 8.35 Characteristic of Seasonal Autoregressive Integrated Moving Average models for dengue hemorrhagic fever and climatic variables in Deli Serdang district …..…….. 341

Table 8.36 Regression coefficient of climatic data on monthly dengue hemorrhagic fever in Deli Serdang district…… 342

LIST OF FIGURES

Page

Figure 2.1. The dengue viral genome …… 17

Figure 2.2. Aedes aegypti mosquito ……... 18

Figure 2.3. Metamorphosis of Aedes aegypti ……. 19

Figure 2.4. Chain of dengue infection …… 21

Figure 2.5. Pathogenesis of dengue virus infection …… 34

Figure 2.6. Steps in surveillance activities ……. 43

Figure 3.1 Map of North Sumatera Province ……. 55

Figure 3.2 Map of district high and low dengue hemorrhagic fever incidence in North Sumatera Province…… 56

Figure 3.3. Flow chart of the methodology in five study designs ……. 63

Figure 4.1 Flow chart of selection of study area in exploratory study…. 67

Figure 4.2 The selected districts in study area……. 67

Figure 4.2.a The selected health facilities In Medan …… 67

Figure 4.2.b The selected health facilities in Pematang Siantar……. 68

Figure 4.2.c The selected health facilities in Tebing Tinggi …… 68

Figure 4.2.d The selected health facilities in Langkat ……. 69

Figure 4.2.e The selected health facilities in Asahan …….. 69

Figure 4.2.f The selected health facilities In Deli Serdang …… 70

Figure 4.3 Kedai Durian Health Facility …….. 73

Figure 4.4 The structure and flow of reporting for the surveillance system for dengue hemorrhagic fever…… 75

Figure 4.5 The Mechanism of surveillance system at health facility… 79

Figure 5.1 Flow chart of case cohort study…….. 123

Figure 5.2 Verification of cases admitted to Pringadi Hospital Medan District…….. 124

Figure 5.3 Detection of IgG/IgM for dengue in sub-cohort in Medan District ……. 125

Figure 5.4 Procedure for detection IgG/IgM by Panbio Dengue Duo cassette ……. 126

Figure 5.5 Detection IgG/IgM in the serum compared to Whole blood… 137

Figure 5.6 Scree plot of eigenvalue for knowledge ……... 140

Figure 5.7 Scree plot of eigenvalue for attitude …… 145

Figure 5.8 Area under the ROC curve for knowledge ……. 159

Figure 5.9 Area under the ROC curve for attitude …….. 168

Figure 6.1 Flow chart of Comparative Study…… 185

Figure 6.2 Area under the ROC Curve of Multivariate Logistic Regression Model in Comparative Study…… 205

Figure 7.1 Design of the entomological study…… 221

Figure 7.2 Type of water containera in and around the house…….. 228

Figure 7.3 Tools that were used in larval survey…… 228

Figure 7.4 Activity in larval survey…… 229

Figure 7.5 Collection of Aedes mosquitoes using aspirator in adult survey. 230

Figure 7.6 Examination of Aedes larvae and Aedes mosquitoes…….. 231

Figure 7.7-7.15 Distribution pattern of Aedes Larvae and Aedes Mosquito ……... 246

Figure 8.1 Map of North Sumatera Province …… 266

Figure 8.2 Study area in high incidence districts ……... 268

Figure 8.3 Study area in low incidence districts …… 269

Figure 8.4.The monthly number of dengue hemorrhagic fever cases in Medan from 2003 to 2011 …….. 273

Figure 8.4a.The monthly fluctuation of temperatures in Medan from 2003 to 2011 …….. 273

Figure 8.4b.The monthly fluctuation of average humidity in Medan from 2003 to 2011 …….. 273

Figure 8.4c.The monthly fluctuation of rainfall in Medan from 2003 to 2011 …….. 273

Figure 8.4d.The monthly fluctuation of rainy days in Medan from 2003 to 2011 ……. 273

Figure 8.5 Time series plot of number of dengue hemorrhagic fever cases in Medan from 2003 to 2011…… 276

Figure 8.5a. ACF of dengue hemorrhagic fever Cases……. 276

Figure 8.5b. PACF of dengue hemorrhagic fever Cases…….. 276

Figure 8.5c. ACF after differencing …… 277

Figure 8.5d. PACF after differencing …..…….. 277

Figure 8.5e. Analysis of residual on ACF……... 277

Figure 8.5f. Analysis of residual on PACF ……. 277

Figure 8.6 Time series plot of rainfall in Medan from 2003 to 2011….. 277

Figure 8.6a. ACF of rainfall ……... 278

Figure 8.6b. PACF of rainfall …….. 278

Figure 8.6c. ACF after differencing …… 278

Figure 8.6d. PACF after differencing …..…….. 278

Figure 8.6e. Analysis of residual on ACF…… 278

Figure 8.6f. Analysis of residual on PACF ……. 278

Figure 8.7 Time series plot of rainy days in Medan from 2003 to 2011……. 278

Figure 8.7a. ACF of rainy Days …….. 279

Figure 8.7b. PACF of rainy Days …… 279

Figure 8.7c. ACF after differencing …… 279

Figure 8.7d. PACF after differencing …..…….. 279

Figure 8.7e. Analysis of residual on ACF……... 279

Figure 8.7f. Analysis of residual on PACF ……. 279

Figure 8.8 Time series plot of minimum temperature in Medan from 2003 to 2011…….. 279

Figure 8.8a. ACF of minimum Temperature ……. 279

Figure 8.8b. PACF of minimum Temperature …… 280

Figure 8.8c. ACF after Differencing …….. 280

Figure 8.8d. PACF after Differencing …..……. 280

Figure 8.8e. Analysis of residual on ACF…… 280

Figure 8.8f. Analysis of residual on PACF…….. 280

Figure 8.9 Time series plot of maximum temperature in Medan from 2003 to 2011……. 280

Figure 8.9a. ACF of maximum Temperature …….. 281

Figure 8.9b. PACF of maximum Temperature …… 281

Figure 8.9c. ACF after differencing …….. 281

Figure 8.9d. PACF after differencing …..……. 281

Figure 8.9e. Analysis of residual on ACF…….. 281

Figure 8.9f. Analysis of residual on PACF …… 281

Figure 8.10 Time series plot of average temperature in Medan from 2003 to 2011……. 281

Figure 8.10a. ACF of average temperature …….. 282

Figure 8.10b. PACF of average temperature ……. 282

Figure 8.10c. ACF after differencing …… 282

Figure 8.10d. PACF after differencing …..…….. 282

Figure 8.10e. Analysis of residual on ACF…….. 282

Figure 8.10f. Analysis of Residual on PACF …….. 282

Figure 8.11 Time series plot of average humidity in Medan from 2003 to 2011…… 282

Figure 8.11a. ACF of average humidity ……. 283

Figure 8.11b. PACF of average humidity …… 283

Figure 8.11c. ACF after differencing …….. 283

Figure 8.11d. PACF after differencing …..……. 283

Figure 8.11e. Analysis of residual on ACF…….. 283

Figure 8.11f. Analysis of residual on PACF …… 283

Figure 8.12.The monthly number of dengue hemorrhagic fever cases In Pematang Siantar from 2003 to 2011 …… 286

Figure 8.12a.The monthly fluctuation of temperatures in Pematang Siantar from 2003 to 2011 …… 286

Figure 8.12b.The monthly fluctuation of average humidity in Pematang Siantar from 2003 to 2011 ……. 286

Figure 8.12c.The monthly fluctuation of rainfall in Pematang Siantar from 2003 to 2011 …….. 287

Figure 8.12d.The monthly fluctuation of rainy days in Pematang Siantar from 2003 to 2011 …… 287

Figure 8.13 Time series plot of number of dengue hemorrhagic fever cases in Pematang Siantar from 2003 to 2011…….. 289

Figure 8.13a. ACF of dengue hemorrhagic fever cases…… 289

Figure 8.13b. PACF of dengue hemorrhagic fever cases……. 289

Figure 8.13c. ACF after differencing ……. 289

Figure 8.13d. PACF after differencing …..…… 289

Figure 8.13e. Analysis of residual on ACF……. 290

Figure 8.13f. Analysis of residual on PACF …….. 290

Figure 8.14 Time series plot of rainfall in Pematang Siantar from 2003 to 2011…….. 290

Figure 8.14a. ACF of rainfall ……. 290

Figure 8.14b. PACF of rainfall…… 290

Figure 8.14c. Analysis of residual on ACF……. 291

Figure 8.14d. Analysis of residual on PACF …….. 291

Figure 8.15 Time series plot of rainy days in Pematang Siantar from 2003 to 2011…….. 291

Figure 8.15a. ACF of rainy Days …… 291

Figure 8.15b. PACF of rainy Days…….. 291

Figure 8.15c. . ACF after differencing …… 291

Figure 8.15d. PACF after differencing …..……. 291

Figure 8.15e. Analysis of residual on ACF……. 292

Figure 8.15f. Analysis of residual on PACF …… 292

Figure 8.16 Time series plot of minimum temperature in Pematang Siantar from 2003 to 2011……. 292

Figure 8.16a. ACF of minimum Temperature…..…….. 292

Figure 8.16b. PACF of minimum Temperature …… 292

Figure 8.16c. ACF after differencing …… 292

Figure 8.16d. PACF after differencing …..…….. 292

Figure 8.16e. Analysis of residual on ACF…… 293

Figure 8.16f. Analysis of residual on PACF ……. 293

Figure 8.17 Time series plot of maximum temperature in Pematang Siantar from 2003 to 2011…… 293

Figure 8.17a. ACF of maximum temperature …… 293

Figure 8.17b. PACF of maximum temperature ……. 293

Figure 8.17c. ACF after differencing …… 293

Figure 8.17d. PACF after differencing …..…….. 293

Figure 8.17e. Analysis of residual on ACF…… 293

Figure 8.17f. Analysis of residual on PACF ……. 293

Figure 8.18 Time series plot of average temperature in Pematang Siantar from 2003 to 2011…….. 294

Figure 8.18a. ACF of average temperature…… 294

Figure 8.18b. PACF of average temperature …… 294

Figure 8.18c. ACF after differencing …… 294

Figure 8.18d. PACF after differencing …..…….. 294

Figure 8.18e. Analysis of residual on ACF…… 294

Figure 8.18f. Analysis of residual on PACF ……. 294

Figure 8.19 Time series plot of average humidity in Pematang Siantar from 2003 to 2011……. 294

Figure 8.19a. ACF of average humidity …… 295

Figure 8.19b. PACF of average humidity ……. 295

Figure 8.19c. ACF after differencing …… 295

Figure 8.19d. PACF after differencing …..…….. 295

Figure 8.19e. Analysis of residual on ACF…….. 295

Figure 8.19f. Analysis of residual on PACF …… 295

Figure 8.20.The monthly number of dengue hemorrhagic fever cases in Tebing Tinggi from 2003 to 2011 …….. 298

Figure 8.20a.The monthly fluctuation of temperatures in Tebing Tinggi from 2003 to 2011 …… 298

Figure 8.20b.The monthly fluctuation of average humidity in Tebing Tinggi from 2003 to 2011 …….. 298

Figure 8.20c.The monthly fluctuation of rainfall in Tebing Tinggi from 2003 to 2011 ……. 298

Figure 8.20d.The monthly fluctuation of rainy days in Tebing Tinggi from 2003 to 2011 ……. 298

Figure 8.21 Time series plot of number of dengue hemorrhagic fever cases in Tebing Tinggi from 2003 to 2011…….. 301

Figure 8.21a. ACF of dengue hemorrhagic fever cases…… 301

Figure 8.21b. PACF of dengue hemorrhagic fever cases……. 301

Figure 8.21c. ACF after differencing …….. 301

Figure 8.21d. PACF after differencing …..…… 301

Figure 8.21e. Analysis of residual on ACF……. 301

Figure 8.21f. Analysis of residual on PACF …….. 301

Figure 8.22 Time series plot of rainfall in Tebing Tinggi from 2003 to 2011…….. 302

Figure 8.22a. ACF of rainfall ……. 302

Figure 8.22b. PACF of rainfall…… 302

Figure 8.22c. ACF after differencing ……. 302

Figure 8.22d. PACF after differencing …..…… 302

Figure 8.22e. Analysis of residual on ACF……. 302

Figure 8.22f. Analysis of residual on PACF …….. 302

Figure 8.23 Time series plot of rainy days in Tebing Tinggi from 2003 to 2011……. 303

Figure 8.23a. ACF of rainy days…… 303

Figure 8.23b. PACF of rainy days ……... 303

Figure 8.23c. . ACF after differencing ……. 303

Figure 8.23d. PACF after differencing …..……. 303

Figure 8.23e. Analysis of residual on ACF…….. 303

Figure 8.23f. Analysis of residual on PACF …… 303

Figure 8.24 Time series plot of maximum temperature in Tebing Tinggi from 2003 to 2011…….. 303

Figure 8.24a. ACF of maximum temperature ……. 304

Figure 8.24b. PACF of maximum temperature …….. 304

Figure 8.24c. ACF after differencing ……. 304

Figure 8.24d. PACF after differencing …..……. 304

Figure 8.24e. Analysis of residual on ACF…….. 304

Figure 8.24f. Analysis of residual on PACF …… 304

Figure 8.25 Time series plot of minimum temperature in Tebing Tinggi from 2003 to 2011…… 304

Figure 8.25a. ACF of minimum temperature….…….. 304

Figure 8.25b. PACF of minimum temperature …… 304

Figure 8.25c. ACF after differencing ……... 305

Figure 8.25d. PACF after differencing …..…….. 305

Figure 8.25e. Analysis of residual on ACF…… 305

Figure 8.25f. Analysis of residual on PACF …… 305

Figure 8.26 Time series plot of average temperature in Tebing Tinggi from 2003 to 2011……. 305

Figure 8.26a. ACF of average temperature…… 305

Figure 8.26b. PACF of average temperature …… 305

Figure 8.26c. ACF after differencing …….. 305

Figure 8.26d. PACF after differencing …..……. 305

Figure 8.26e. Analysis of residual on ACF…….. 306

Figure 8.26f. Analysis of residual on PACF …… 306

Figure 8.27 Time series plot of average humidity in Tebing Tinggi from 2003 to 2011…… 306

Figure 8.27a. ACF of average humidity …….. 306

Figure 8.27b. PACF of average humidity …… 306

Figure 8.27c. ACF after differencing ……. 306

Figure 8.27d. PACF after differencing …..……. 306

Figure 8.27e. Analysis of residual on ACF…….. 306

Figure 8.27f. Analysis of residual on PACF …… 306

Figure 8.28.The monthly number of dengue hemorrhagic fever cases
In Langkat from 2003 to 2011 ……. 309

Figure 8.28a.The monthly fluctuation of temperatures in Langkat
from 2003 to 2011 …… 310

Figure 8.28b.The monthly fluctuation of average humidity in
Langkat from 2003 to 2011 …… 310

Figure 8.28c.The monthly fluctuation of rainfall in Langkat
from 2003 to 2011 …….. 310

Figure 8.28d.The monthly fluctuation of rainy days in Langkat
from 2003 to 2011 …… 310

Figure 8.29. Time series plot of dengue hemorrhagic fever cases
in Langkat from 2003 to 2011 ……. 312

Figure 8.29a. ACF of dengue hemorrhagic fever cases …….. 313

Figure 8.29b. PACF of dengue hemorrhagic fever cases …… 313

Figure 8.29c. ACF after differencing ……. 313

Figure 8.29d. PACF after differencing ……. 313

Figure 8.29e. Analysis residual on ACF…… 313

Figure 8.29f. Analysis residual on PACF……. 313

Figure 8.30 Time series plot of rainfall in Langkat from 2003 to 2011……. 313

Figure 8.30a. ACF of rainfall …….. 314

Figure 8.30b. PACF of rainfall……. 314

Figure 8.30c. ACF after differencing …….. 314

Figure 8.30d. PACF after differencing …..……. 314

Figure 8.30e. Analysis of residual on ACF…….. 314

Figure 8.30f. Analysis of residual on PACF …… 314

Figure 8.31 Time series plot of rainy days in Langkat from 2003 to 2011…… 314

Figure 8.31a. ACF of rainy days…… 314

Figure 8.31b. PACF of rainy days …… 314

Figure 8.31c. ACF after differencing …… 315

Figure 8.31d. PACF after differencing …..……. 315

Figure 8.31e. Analysis of residual on ACF…….. 315

Figure 8.31f. Analysis of residual on PACF …… 315

Figure 8.32 Time series plot of minimum temperature in Langkat from 2003 to 2011…… 315

Figure 8.32a. ACF of minimum temperature….…….. 315

Figure 8.32b. PACF of minimum temperature …… 315

Figure 8.32c. ACF after differencing …… 315

Figure 8.32d. PACF after differencing …..……. 315

Figure 8.32e. Analysis of residual on ACF…….. 316

Figure 8.32f. Analysis of residual on PACF …… 316

Figure 8.33 Time series plot of maximum temperature in Langkat from 2003 to 2011…….. 316

Figure 8.33a. ACF of maximum temperature ……. 316

Figure 8.33b. PACF of maximum temperature …….. 316

Figure 8.33c. ACF after differencing ……. 316

Figure 8.33d. PACF after differencing …..……. 316

Figure 8.33e. Analysis of residual on ACF…….. 316

Figure 8.33f. Analysis of residual on PACF …… 316

Figure 8.34 Time series plot of average temperature in Langkat from 2003 to 2011…… 317

Figure 8.34a. ACF of average temperature……. 317

Figure 8.34b. PACF of average temperature ……. 317

Figure 8.34c. ACF after differencing ……. 317

Figure 8.34d. PACF after differencing …..……. 317

Figure 8.34e. Analysis of residual on ACF…….. 317

Figure 8.34f. Analysis of residual on PACF …… 317

Figure 8.35 Time series plot of average humidity in Langkat from 2003 to 2011…… 317

Figure 835a. ACF of average Humidity ……. 318

Figure 8.35b. PACF of average humidity …… 318

Figure 8.35c. ACF after differencing …….. 318

Figure 8.35d. PACF after differencing …..……. 318

Figure 8.35e. Analysis of residual on ACF…….. 318

Figure 8.35f. Analysis of residual on PACF …… 318

Figure 8.36.The monthly number of dengue hemorrhagic fever cases in Asahan from 2003 to 2011 ……. 321

Figure 8.36a.The monthly fluctuation of temperatures in Asahan from 2003 to 2011 ……. 321

Figure 8.36b.The monthly fluctuation of average humidity in Asahan from 2003 to 2011 ……. 321

Figure 8.36c.The monthly fluctuation of rainfall in Asahan from 2003 to 2011 ……. 322

Figure 8.36d.The monthly fluctuation of rainy days in Asahan from 2003 to 2011 …… 322

Figure 8.37. Time series plot of number of dengue hemorrhagic fever cases in Asahan from 2003 to 2011…… 324

Figure 8.37a. ACF of dengue hemorrhagic fever cases…….. 324

Figure 8.37b. PACF of dengue hemorrhagic fever cases…… 324

Figure 8.37c. ACF after differencing ……. 324

Figure 8.37d. PACF after differencing …..……. 324

Figure 8.37e. Analysis of residual on ACF…….. 324

Figure 8.37f. Analysis of residual on PACF …… 324

Figure 8.38 Time series plot of rainfall in Asahan from 2003 to 2011…… 325

Figure 8.38a. ACF of rainfall …….. 325

Figure 8.38b. PACF of rainfall…… 325

Figure 8.38c. ACF after differencing ……. 325

Figure 8.38d. PACF after differencing …..……. 325

Figure 8.38e. Analysis of residual on ACF…….. 325

Figure 8.38f. Analysis of residual on PACF …… 325

Figure 8.39 Time series plot of rainy days in Asahan from 2003 to 2011…… 326

Figure 8.39a. ACF of rainy days…….. 326

Figure 8.39b. PACF of rainy days …… 326

Figure 8.39c. . ACF after differencing ……. 326

Figure 8.39d. PACF after differencing …..……. 326

Figure 8.39e. Analysis of residual on ACF…….. 326

Figure 8.39f. Analysis of residual on PACF …… 326

Figure 8.40 Time series plot of minimum temperature in Asahan from 2003 to 2011…… 326

Figure 8.40a. ACF of minimum temperature….…….. 327

Figure 8.40b. PACF of minimum temperature …….. 327

Figure 8.40c. ACF after differencing ……. 327

Figure 8.40d. PACF after differencing …..……. 327

Figure 8.40e. Analysis of residual on ACF…….. 327

Figure 8.40f. Analysis of residual on PACF …… 327

Figure 8.41 Time series plot of maximum temperature in Asahan from 2003 to 2011…….. 327

Figure 8.41a. ACF of maximum temperature ……. 327

Figure 8.41b. PACF of maximum temperature …….. 327

Figure 8.41c. ACF after differencing ……. 328

Figure 8.41d. PACF after differencing …..……. 328

Figure 8.41e. Analysis of residual on ACF…….. 328

Figure 8.41f. Analysis of residual on PACF …… 328

Figure 8.42 Time series plot of average temperature in Asahan from 2003 to 2011…… 328

Figure 8.42a. ACF of average temperature……. 328

Figure 8.42b. PACF of average temperature ……. 328

Figure 8.42c. ACF after differencing ……. 328

Figure 8.42d. PACF after differencing …..……. 328

Figure 8.42e. Analysis of residual on ACF…….. 329

Figure 8.42f. Analysis of residual on PACF …… 329

Figure 8.43 Time series plot of average humidity in Asahan from 2003 to 2011…… 329

Figure 843a. ACF of average humidity ……. 329

Figure 8.43b. PACF of average humidity ……. 329

Figure 8.43c. ACF after differencing ……. 329

Figure 8.43d. PACF after differencing …..……. 329

Figure 8.43e. Analysis of residual on ACF…….. 329

Figure 8.43f. Analysis of residual on PACF …… 329

Figure 8.44.The monthly number of dengue hemorrhagic fever cases in Deli Serdang from 2003 to 2011 …… 332

Figure 8.44a.The monthly fluctuation of temperatures in Deli Serdang from 2003 to 2011 ……. 333

Figure 8.44b.The monthly fluctuation of average humidity in Deli Serdang from 2003 to 2011 …… 333

Figure 8.44c.The monthly fluctuation of rainfall in Deli Serdang from 2003 to 2011 ……. 333

Figure 8.44d.The monthly fluctuation of rainy days in Deli Serdang from 2003 to 2011 …… 333

Figure 8.45 Time series plot of number of dengue hemorrhagic fever cases in Deli Serdang from 2003 to 2011…… 335

Figure 8.45a. ACF of dengue hemorrhagic fever cases…….. 335

Figure 8.45b. PACF of dengue hemorrhagic fever cases…… 335

Figure 8.45c. ACF after differencing ……. 336

Figure 8.45d. PACF after differencing …..……. 336

Figure 8.45e. Analysis of residual on ACF…….. 336

Figure 8.45f. Analysis of residual on PACF…… 336

Figure 8.46 Time series plot of rainfall in Deli Serdang from 2003 to 2011…… 336

Figure 8.46a. ACF of rainfall …….. 336

Figure 8.46b. PACF of rainfall…… 336

Figure 8.46c. ACF after differencing ……. 337

Figure 8.46e. Analysis of residual on ACF…….. 337

Figure 8.46f. Analysis of residual on PACF …… 337

Figure 8.47 Time series plot of rainy days in Deli Serdang from 2003 to 2011…… 337

Figure 8.47a. ACF of rainy days…….. 337

Figure 8.47b. PACF of rainy days …… 337

Figure 8.47c. Analysis of residual on ACF…….. 337

Figure 8.47d. Analysis of residual on PACF …… 337

Figure 8.48 Time series plot of minimum temperature in Deli Serdang from 2003 to 2011…… 338

Figure 8.48a. ACF of minimum temperature…..…….. 338

Figure 8.48b. PACF of minimum temperature …….. 338

Figure 8.48c. ACF after differencing ……. 338

Figure 8.48d. PACF after differencing …..……. 338

Figure 8.48e. Analysis of residual on ACF…….. 338

Figure 8.48f. Analysis of residual on PACF …… 338

Figure 8.49 Time series plot of maximum temperature in Deli Serdang from 2003 to 2011…… 338

Figure 8.49a. ACF of maximum Temperature ……. 339

Figure 8.49b. PACF of maximum Temperature …….. 339

Figure 8.49c. ACF after differencing ……. 339

Figure 8.49d. PACF after differencing …..……. 339

Figure 8.49e. Analysis of residual on ACF…….. 339

Figure 8.49f. Analysis of Residual on PACF …… 339

Figure 8.50 Time series plot of average temperature in Deli Serdang from 2003 to 2011…… 339

Figure 8.50a. ACF of average temperature……. 340

Figure 8.50b. PACF of average temperature ……. 340

Figure 8.50c. ACF after differencing ……. 340

Figure 8.50d. PACF after differencing …..……. 340

Figure 8.50e. Analysis of residual on ACF…….. 340

Figure 8.50f. Analysis of residual on PACF …… 340

Figure 8.51 Time series plot of average humidity in Deli Serdang from 2003 to 2011…… 340

Figure 851a. ACF of average humidity ……. 340

Figure 8.51b. PACF of average humidity ……. 340

Figure 8.51c. ACF after differencing ……. 340

Figure 8.51d. PACF after differencing …..……. 340

Figure 8.51e. Analysis of residual on ACF…….. 341

Figure 8.51f. Analysis of residual on PACF …… 341

LIST OF ABBREVIATIONS

WHO	:	World Health Organization
DHF	:	Dengue Hemorrhagic Fever
DSS	:	Dengue Shock Syndrome
DF	:	Dengue Fever
JD	:	Job Description
HIDs	:	High Incidence District
LIDs	:	Low Incidence District
KAP	:	Knowledge Attitude Practice
HF	:	Health Facility
H	:	Hospital
MOH	:	Ministry of Health
DHO	:	District Health Office
OHS	:	Other Health Sector
WB	:	Whole Blood
RNA	:	Ribonucleid Acid
IgG	:	Immunoglobulin G
IgM	:	Immunoglobulin M
HI	:	House index
CI	:	Container index
BI	:	Breteau index
AHI	:	Adult house index
RR	:	Resting rate
AD	:	Adult density

NCCLS : National Comitte for Clinical Laboratory Standard

SARIMA : Seasonal Autoregressive integrated Moving average

ADE : Antibody Dependent Enhancement

NAATs : Nucleid Acid Amplication Test

RT-PCR : Reverse Transcriptase Polimerase Chain Reaction

ELISA : Enzyme-linked Immunosorbent assay

NS1 : Nonstructural protein

TNF-A : Tumor necrosis Factor Alpha

PAF : Platelet Activating Factor

IFN : Interferon

IL : Interleukin

NO : Nitric oxide

EIP : Extrinsic incubation period

REKOMENDASI STRATEGI UNTUK PENCEGAHAN DAN KAWALAN MORBIDITI TINGGI UNTUK DEMAM DENGGI BERDARAH DI PROPINSI SUMATERA UTARA

ABSTRAK

Latar Belakang : Insiden demam denggi berdarah (DHF) di Sumatera Utara kekal tinggi, meskipun pelbagai usaha dilakukan untuk mengawalnya.

Objektif: Kajian ini bertujuan untuk mendokumentasikan maklumat tentang kecukupan sistem surveilan semasa bagi DHF di Indonesia dan faktor-faktor yang yang menyumbang ke arah peningkatan kes DHF. Ia nya nanti akan digunakan untuk merekomen strategi pencegahan dan kawalan DHF di Sumatera Utara.

Bahan dan Kaedah: Lima reka bentuk kajian digunakan dalam kajian ini. Dalam kajian penerokaan, kesemua kaki tangan utama yang terlibat dalam sistem pengawasan bagi demam denggi berdarah di peringkat daerah dan fasiliti kesihatan di enam daerah telah ditemuramah untuk mengenalpasti fungsi dan prestasi sistem surveilan. Dalam kajian kes kohort, melibatkan 682 kes dan subkohort dengan nisbah 1: 1. Analisis *Simple dan Multiple regresi logistic* digunakan untuk menentukan faktor-faktor yang berkaitan dengan DHF. Untuk kajian keratan rentas perbandingan isi rumah di daerah dengan kes tinggi dan rendah telah dipilih melalui persampelan berbilang peringkat. Lagi sekali analisis *Simple dan Multiple regresi logistic* digunakan untuk menentukan faktor-faktor yang berkaitan dengan demam denggi berdarah di daerah dengan kejadian yang tinggi. Dalam kajian entomologi, *Independent T test* dan *Two Way Anova* digunakan untuk menentukan kesan bekas yang positif larvae ke atas DHF sementara bagi indeks larvae dan

Aedes dewasa analisis *Simple dan Multiple regresi logistic* digunakan. Kajian cuaca menggunapakai data cuaca bulanan selama 9 tahun (2003-2011). *Pearson correlati*on digunakan untuk menentukan hubungan cuaca dan DHF dan *Time series regression* digunakan untuk menentukan impak cuaca ke atas insiden DHF. Seasonal Autoregressive Moving Average (SARIMA) model dibina untuk meramal kejadian DHF.

Keputusan: Struktur sistem surveilan untuk DHF adalah bagus tetapi pelaksanaannya tidak optimum dengan kekurangan major yang termasuk ketiadaan garis panduan, kekurangan sumber, dan kelemahan ketara dalam fungsi utama dan sokongan. Faktor - faktor sosio-budaya dan alam sekitar dikaji melalui kajian kes kohort dan kajian keratan rentas perbandingan. Faktor yang signifikan dengan insiden DHF termasuk pengalaman dengan DHF dalam keluarga, sejarah perjalanan, tempoh penginapan, kekerapan bekas air pembersihan, kekerapan pembersihan pelupusan sampah, pendidikan, pengetahuan, amalan dalam langkah pencegahan, sumber air minuman, gaya rumah dan rumah dengan longkang. Indeks larva *Aedes* dan nyamuk dewasa diatas tahap kritikal terutamanya di daerah dengan insiden DHF yang tinggi dengan house indeks (indeks rumah) boleh digunakan untuk meramal jangkitan denggi. Faktor cuaca yang termasuk jumlah hujan, hari hujan, suhu dan kelembaban relatif adalah berikatan dengan insiden DHF. Model SARIMA $(0,1,1)(0,1,1)_{12}$ berupaya meramalkan kejadian DHF.

Kesimpulan: Fungsi dan keupayaan sistem surveilan bagi DHF perlu diperkuatkan dalam semua aspek. Faktor sosio-budaya dan persekitaran yang berkait dengan DHF perlu ditangani dan dikawal. Langkah perlu diambil untuk

menghapuskan atau mengurangkan kepadatan vektor *Aedes*. Faktor cuaca patut diintegrasi didalam program kawalan dan pencegahan DHF nasional.

RECOMMENDATION STRATEGIES FOR THE PREVENTION AND CONTROL OF HIGH MORBIDITY OF DENGUE HEMORRHAGIC FEVER IN NORTH SUMATERA PROVINCE

ABSTRACT

Background: The incidence of dengue hemorrhagic fever (DHF) in North Sumatera Province remains high despite effort to control it.

Objectives : This study aimed to document information about the adequacy of the current Indonesia surveillance system for DHF and factors responsible for high DHF transmission. These will be used for recommending strategies for the prevention and control for DHF in North Sumatera Province.

Material and Methods: Five study designs were adopted in this study. In the exploratory study, all key personnels involved in the surveillance system for DHF at the district and health facility levels in the selected six districts were interviewed to determine the function and performance of the surveillance system. The case cohort study recruited a total of 682 respondents with case: subcohort ratio 1:1. S*imple and Multiple logistic reg*ression were applied to determine the factors associated with DHF. For the comparative cross sectional study, 688 households both in high and low incidence district were selected using multistage sampling. *Simple and Multiple logistic regression* were again applied to determine the factors associated with DHF among the households in districts with high incidence. In the entomology study, *Independent T test* and *Two Way Anova* were used to determine the effect of larvae positive containers on DHF transmission, whereas for larvae and adult indices *Simple and Multiple logistic regression* were applied. The

climatic study utilises monthly a years climatic (2003-2011) secondary data. The relationship between climatic and dengue hemorrhagic fever incidence was determined by *Pearson correlation* and the impact of climates on DHF incidence by *Time series regression*. *Seasonal Autoregressive Integrated Moving Average* (SARIMA) model was then developed to predict the occurrence of DHF.

Results : The structure of DHF surveillance system was good but suboptimum with major deficiencies that include unavailability of guidelines, insufficient resources and poor core and supportive functions. Socio-cultural and environmental factors associated with DHF incidence were investigated through case–cohort and comparative cross sectional studies. Significant factors include experience with DHF in family, travelling history, length of stay, frequency of cleaning water container, frequency of cleaning garbage disposal, education, knowledge, practices in preventive measure, source of drinking water, house style and house with gutter. *Aedes* larvae and adult indices were above the critical level especially in the high incidence districts with house indices as the predictor for dengue transmission. Climatic factors that include rainfall, rainy days, temperature and relative humidity were significantly associated with DHF incidence. SARIMA model $(0,1,1)(0,1,1)^{12}$ was able to predict DHF occurrence.

Conclusion: The existing surveillance system for DHF need to be strengthened in every aspect. Socio-cultural and environmental factors associated with DHF should be addressed and controlled. Measures should be taken to eliminate or being down the density of *Aedes* vectors. Climatic factors should be integrated in the national prevention and control program for DHF.

CHAPTER 1

INTRODUCTION

1.1 Background

Dengue hemorrhagic fever (DHF) is considered to be the most important public health problem in many tropical and subtropical countries around the world. The disease has gained recognition in many countries and currently more than 100 countries are endemic with dengue virus infection (Guzman and Istúriz, 2010; Guzman *et al.*, 2010).

DHF becomes the leading cause of morbidity with 3.6 billion people living in areas of high risk for dengue infection (Wilder-Smith., *et al* 2012). Worldwide 50 to 100 million cases of dengue fever occur every year and 250,000 to 500,000 cases were DHF resulting in approximately 25,000 death (Guzman *et al.*, 2010). Recent studies suggested that there were about 230 million infections worldwide (Wilder-Smith *et al.*, 2012). However, the true incidence is still not known (Guzman *et al.*, 2010).

World health organization (WHO) reported that the annual average number of DHF cases had increased. For the period 2000-2004s, the number of DHF cases was 925,896 almost doubled compared that for 1990-1999s (Guzman *et al.*, 2010). While in 2010, there were 96 million dengue infections estimated worldwide with the Americas contributed 14 % and Africa 16 % of the infection (Bhatt *et al.*, 2013).

Asia ranked first in the number of patients with dengue fever each year and contributes as much as 70% of infections worldwide (Bhatt *et al.*, 2013). Dengue hemorrhagic fever is a leading cause of hospitalization among children with case fatality rate (CFR) exceeding 5% in some areas. The first case of dengue was reported in Penang, Malaysia in 1901 (Poovaneswari,1993). Then the disease spread to the Philippines (1953), Cambodia (1961), Calcuta (1963), Sri lanka (1966), Indonesia (1968), and Singapore. In Singapore dengue cases has been reported since the 1990s, with a peak in 2005 giving the incidence of dengue cases at 335 per 100,000 population (Carrasco *et al.*, 2011). From 1968 to 2009, WHO noted Indonesia as the country with the highest dengue cases in Southeast Asia and the second highest in the world after Brazil (Organization, 2012).

In Indonesia, DHF is one of the emerging diseases with an increased incidence throughout the year. The disease was first recognized in 1968 in Surabaya and Jakarta with a CFR of 41.3%. Since then, incidence of the disease has increased from 9 cases per 100.000 population in 1992 to 67 per 100.000 population in 2007, and 28 cases per 100.000 population in 2011. Meanwhile CFR had decreased from 2.9% in 1992 to 1.02% in 2007 and 0.73 % in 2011 (Ministry of Health Indonesia, 2012). The districts affected had also increased from 187 districts in 1992 to 337 districts in 2007, and 464 districts in 2010. This emerging disease posed an important public health problem in Indonesia because of its high rate morbidity and mortality mainly among children. Out of 34 provinces, one of the endemic areas is North Sumatera Province (Ministry of Health Indonesia,2010). The latest report by Ministry of Health, North Sumatera Province the third highest for DHF cases (Ministry of Health Indonesia, 2011).

In 2005, DHF incidence in North Sumatera Province ranked 19 with 31 cases per 100.000 population and a CFR of 0.9% (Ministry of Health Indonesia, 2007). DHF was recognized in North Sumatera Province in 1975. Within a 10 year period (2003-2012), incidence rate increased from 8 cases per 100.000 population in 2003 to 24 cases per 100.000 population in 2007 and 35.18 per 100.000 population in 2010 and 18.45 cases per 100.000 population in 2012. While CFR decreased from 2.45% in 2003 to 0.9% in 2007, to 1.0% in 2010 and 0.8% in 2012. However, spread of DHF extended from 24 districts in 2010 to 27 districts in 2011 and 31 districts in 2012 (Provincial Health Office of North Sumatera, 2012).

Out of 25 districts in North Sumatera Province, 16 were dengue endemic districts. They were classified into high and low endemic district based on the incidence data (2007). Medan, Pematang Siantar and Tebing Tinggi districts were classified as high endemic districts. While Langkat, Asahan and Deli Serdang were low endemic districts. Within a 5 year period (2007-2012), incidence rate fluctuated from 88.6 cases per 100.000 population in 2007 to 56.7 cases per 100.000 population in 2012 in Medan, from 291 cases per 100.000 population in 2007 to 260 cases per 100.000 population in 2012 in Pematang Siantar, from 295 cases per 100.000 population in 2007 to 106 cases per 100.000 population in 2012 in Tebing Tinggi, from 10.4 cases per 100.000 population in 2007 to 14.8 cases per 100.000 population in 2012 in Langkat, from 10.6 cases per 100.000 population in 2007 to 31.1 cases per 100.000 population in 2012 in Asahan, and in Deli serdang from 19.68 cases per 100.000 population in 2007 to 32.5 cases per 100.000 population in 2012. Overall the above data shows that the incidence rate of DHF in North Sumatera Province was still high.

Dengue hemorrhagic fever has a public health, social and economic impact. Public health impact is related to the burden of the disease including the number of clinical cases by severity, duration of illness period, quality of life during the illness period, and the number of deaths during the period (Suaya *et al.*, 2007). The public health impact of dengue fever is due to a poor surveillance system, where many cases are under detected and under reported. As a consequence, hospitalization of DHF cases resulted in overloading of DHF patients in hospitals and overworked medical staff. This would eventually lead to the increase in mortality (Kusriastuti and Sutomo, 2005).

The social impact includes the effects of the disease on patients and their family which is associated with the duration of the disease and financial cost. While loss of work productivity, absence from school, instability of family life due to risk of infection, reduction of life expectancy, and social disruptions are indirect social impacts (Kusriastuti and Sutomo, 2005; Carrasco *et al.*, 2011; Wettstein *et al.*, 2012). The economic impact includes expenses when seeking treatment for both hospitalized and out patients cases (Kusriastuti and Sutomo, 2005; Carrasco *et al.*, 2011; Halasa *et al.*, 2012).

Various efforts have been made to reduce morbidity due to dengue fever, but the results have not been as expected. Up to now there is no vaccine or spesific medication for dengue fever and many factors contributing to high incidence occurrence. The problem faced is the high incidence of DHF. Therefore, effective prevention and control measures are necessary in reducing the incidence of DHF and

should be focused on the disease risk factors. It is closely linked to the effective surveillance system that provide accurate information to be used in planning and implementing health intervention for the control of DHF (Baker and Fidler, 2006) and monitoring the progress of interventions to reduce the disease, early detection and initiating investigation and control measures (John *et al*., 2004; Sahal *et al.*, 2009).

The Ministry of Health Indonesia had established DHF as one of the priorities in the prevention and control program of infectious diseases in Indonesia. Therefore, surveillance system was conducted since 1984. In order to understand the whole concept of surveillance system, the Ministry of Health created a guideline for the implementation of a surveillance system for DHF. In 2003, disease integrated surveillance system was introduced both to communicable and non communicable diseases with active and passive approach, and involved health services, hospitals, communities and laboratories (Ministry of Health Indonesia, 2004).

In Indonesia, DHF reporting is regulated by epidemic act (UU Wabah nr 4/1984) and Ministry of Health (regulation nr 560/1989), which states that every case of infectious disease occurs and which could potentially cause an outbreak, then should be reported to the district health authority within 24 hours (Ministry of Health Indonesia, 2005). Surveillance system relies on passive reporting by physician, healthcare provider, hospital, health facility that managed DHF cases. The system depends on the awareness and interest of the medical community. Although the system is relative insensitive, however it is useful in monitoring the trend in dengue transmission (Torres and Castro, 2007).

Health facility as primary health centre and important public health services in Indonesia, especially in the impelementation of surveillance system are bottom-up. Health facilities are expected to provide accurate information that describe the actual public health condition (Ministry of Health Indonesia, 2005). In the surveillance system for DHF, case ascertainment using standard case definition is based on clinical diagnosis and laboratory confirmation. However, not all health facilities have laboratory equipment to perform the test for identifying DHF. Therefore, adequate knowledge of the case definition among health personnels both in the health facilities and at the district health levels is necessary (Kusriastuti and Sutomo, 2005).

In addition to surveillance of cases, vector surveillance is essential in the implementation of dengue fever surveillance to monitor the density of vector mosquitoes. This information could determine outbreak risk and the need for specific vector control to break the chain of disease transmission. However, in North Sumatera Province the implementation of vector surveillance has not been conducted regularly. This certainly affects the accuracy of the information regarding high risk areas and factors associated resulting in less effective control measures for dengue hemorrhagic fever.

In North Sumatera Province, the surveillance system for DHF started in 1993 and was merely for data collection and data reporting. Currently, the implementation of surveillance system is mainly passive reporting. Based on the decision by the Ministry of Health (nr 1116/2003), the surveillance system implementation has been

integrated, however the involvement of laboratory and private health sector is still low. It affects completeness and timeliness reporting from health facilities and hospitals and has impact on the actual number of cases of DHF. In addition, cases ascertainment of DHF based on WHO criteria and most of reported cases were not supported by laboratory confirmation due to the lack of laboratory facilities This also might have impact on the actual number of cases of DHF being reported and the performance of surveillance system.

Based on the North Sumatera Province surveillance report (2007), the completeness and timeliness of reporting from health facilities and hospital are still below of the Ministry of health standard. Completeness of reporting of health facilities and hospitals were 69,7% and 43,14%, while the timeliness in disease reporting was 62,69% and 38,37%, respectively. This result leads to misinterpretation in describing the magnitude of the problem and determining the prevention and control measures for dengue fever.

Effective prevention and control measures are essential in reducing mortality and morbidity of DHF, and they are closely linked to an effective surveillance system that provides accurate information that could be used for planning, implementing and evaluating health intervention. In addition, the effective prevention and control measures for DHF should be focused and based on the disease risk factor. Therefore, the factors associated with the incidence of DHF and deficiencies of surveillance system should be identified. These information is used as the recommendation for an effective surveillance system and successful control for DHF.

1.2 Problem statements

Dengue hemorrhagic fever is one of the major health problems in North Sumatera Province. The incidence of DHF increased annually and remains high. Geographically the district affected increased to 16 endemic areas in 2007.

Dengue hemorrhagic fever as a problem is complex. Many factors contribute to the incidence of DHF including socio-demographic and socio-cultural background, and environmental factors that create potential breeding sites. While geographical and climatic factors that promote vector proliferation, are also responsible. To achieve an effective control measure for dengue fever it requires accurate information both in the number of cases and the factors affecting. However, data on factors associated with the high incidence of dengue fever in North Sumatera Province have not been well known.

Various efforts had been made to reduce morbidity and mortality of DHF. However, the occurence of DHF could not be controlled and the incidence remains high. It was assumed that the prevention and control measure for DHF was not effective but the actual reasons are not known.

An effective prevention and control measures is closely linked to the surveillance system. However, the implementation of existing surveillance system does not seem optimum. The performance of the surveillance system that was reflected by completeness and timeliness of disease reporting was below the standard of Ministry

of Health. In addition, most of the reported cases were based on WHO criteria and not supported by laboratory confirmation. Inadequate knowledge about case definition among health personnel and at the district health level may have impact on the accuracy of number of cases. Although vector surveillance is important to determine high risk area for DHF, vector surveillance has not been regularly conducted.

Since a surveillance system is essential in providing information that could be used in monitoring the disease, implementing health intervention and evaluating, the surveillance system must be effective. This is closely related to the structure, dynamics and attributes of the surveillance system, using the WHO standard as reference. Thus, it is necessary to identify deficiencies of the surveillance system implementation and areas for improvements. In addition, factors that have been associated with DHF incidence should be identified and used in preparing plan for reducing mortality and morbidity of DHF and to establishing priorities for surveillance purposes.

An effective surveillance system provides timely and accurate information that could be used in making decision and implementing health intervention for the control of DHF. This requires integrated surveillance data that include epidemiological, entomological, and environmental data. An optimum surveillance system could predict temporal and spatial risks of DHF.

To achieve an effective prevention and control measures to reduce mortality and morbidity of DHF and also successful control for DHF, an effective surveillance system for DHF is required, and the intervention should be focused and based on the disease risk factors.

1.3 Rationale of the study

The most appropriate approach to reduce the incidence of DHF is by conducting the effective prevention and control measures focusing on the disease risk factors. Risk and factors associated with DF and DHF in North Sumatera has not been officially reported and been made public. As such, it is not known what are the local factors responsible for sustaining high DHF cases in certain districts and area within the North Sumatera Province.

The surveillance system for DHF in North Sumatera Province is assumed to be not optimum but there has not been any report on the effectiveness of the system of DHF for North Sumatera. Thus, proper evaluation is needed to determine its effectiveness and optimize the current performance of the surveillance system. The system requires verification for all the parameters including accurate associated factors for DHF and identification of the structure and process of the surveillance system. This study aims to find, examine and document these information so that they can be used for an effective surveillance system and as a recommendation strategies for the prevention and control for dengue hemorrhagic fever in North Sumatera Province. The result of this study will definitely add information to the body of knowledge and refine the theoretical aspects of DHF surveillance, control and prevention.

1.4 Objectives of Study

1.4.1 General Objective

To study the adequacy of the current Indonesia surveillance system for DHF and to determine the factors responsible for high DHF transmission in North Sumatera Province and then document the information that can be used for recommendation strategies for the prevention and control of high morbidity of dengue hemorrhagic fever in North Sumatera Province.

1.4.2 Spesific Objective

i. To study and explore the current Indonesian surveillance system for DHF based on the attributes used by WHO as the reference standard.
ii. To determine the factors associated with DHF in North Sumatera Province according to respondents socio-demography, socio-cultural factor, knowledge, attitude and practice.
iii. To determine the association between environmental factors and DHF.
iv. To determine the association between entomological factors and DHF.
v. To determine the association between climatic factors and DHF.

1.5 Hypothesis

i. There is an association between socio-demography, socio-cultural, knowledge attitude, practice, and DHF .

ii. There is an association between environmental factors (breeding site, household characteristic) and DHF .

iii. There is an association between entomological factors (larvae density, adult density) and DHF .

iv. There is an associaton between climatic factors (temperature, humidity, rainfall, rainy days) and DHF .

v. Inefficient surveillance system influence the DHF incidence

vi. Effective surveillance prevention and control could reduce DHF incidence

1.6 Conceptual Framework

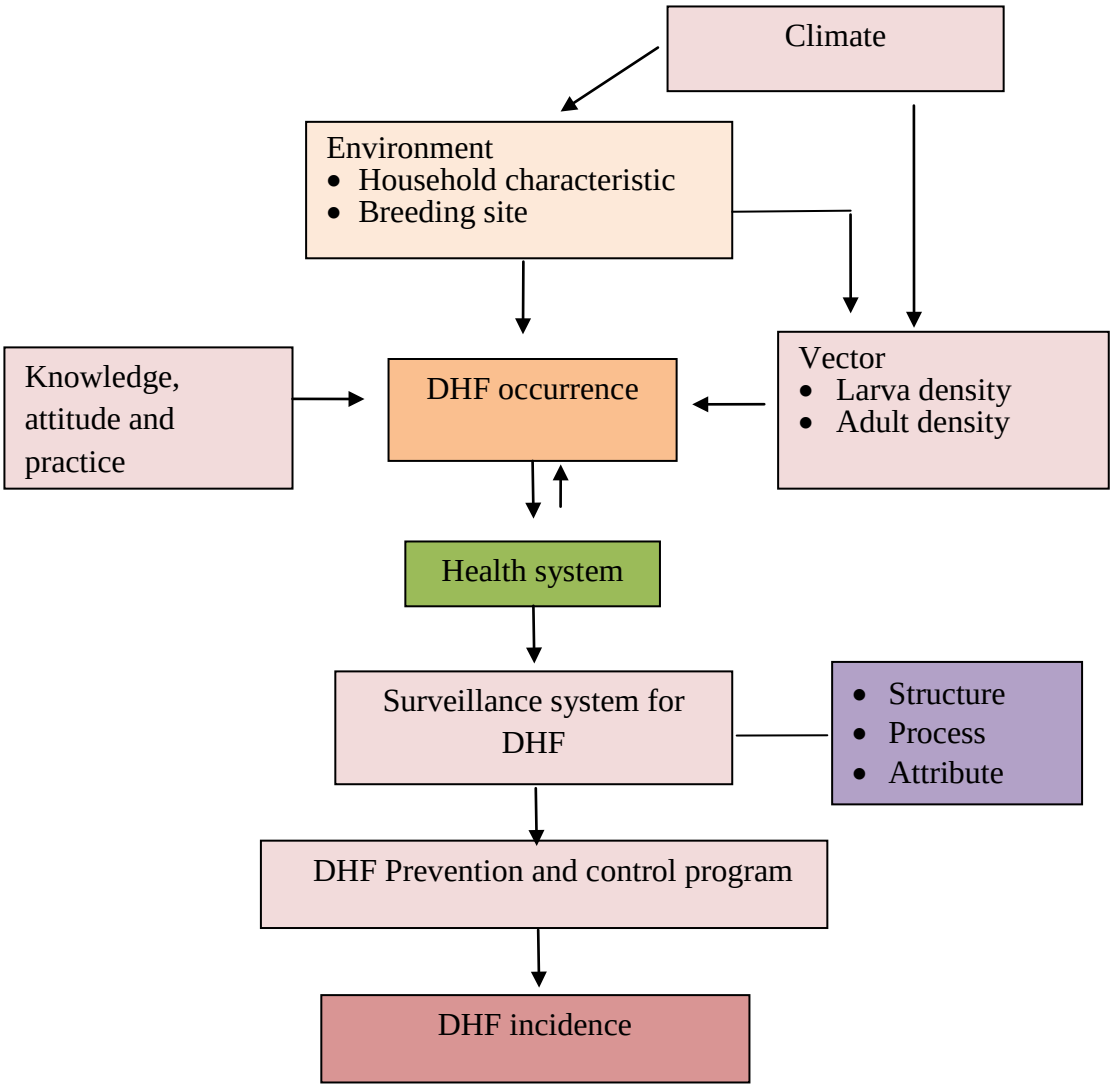

Figure 1.1. Factors associated with DHF occurrence and DHF control program

CHAPTER 2

LITERATURE REVIEW

2.1 The Epidemiology of Dengue Fever and Dengue Hemorrhagic Fever

2.1.1 Dengue Fever and Dengue Hemorrhagic Fever

Dengue infection is one the most important vector-borne disease of human that is caused by dengue virus and transmitted by *Aedes* mosquitoes. The disease becomes health problem around the world (Srikiatkhachorn, 2009; Guzman *et al*., 2010; Whitehorn and Simmons, 2011). The clinical manifestation of dengue infection varies from asymptomatic infection to mild manifestation and severe disease, dengue fever (DF) and dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS) (Lei *et al*., 2001; Guzman and Kouri, 2003; Noisakran and Perng,2008).

Dengue fever also known as breakbone fever is characterized by biphasic fever, severe headache, retro-orbital pain, myalgia, arthralgia, maculopapular rash, lymphadenopathy and leucopenia. DF is defined by the presence of fever and more than 2 of the following symptoms that include headache, retro-orbital pain, myalgia, arthralgia and maculopapular rash. Biphasic fever and maculopapular rash are the characteristics of dengue fever. Although DF is commonly benign and self limiting, a small percentage of dengue patients could develop progressively into DHF or dengue schok syndrome (Lei *et al.*, 2001; Guzman and Kouri, 2003; Noisakran and Perng, 2008).

DHF is characteristized by dengue fever that is accompanied with bleeding manifestation including skin hemorrhages, bleeding nose or gum, and possible internal bleeding. During the febrile phase, hemostasis disorder can occur. Increased vascular permeability causes bleeding manifestation ranging from petechiae to spontaneous bleeding from nose or gastrointestinal tract (Lei *et al*., 2001; Guzman and Kouri, 2003; Srikiatkhachorn, 2009). DHF is defined by fever with thrombocytopenia (platelet count≤100,000 platelet/mm3), hemorrhagic manifestation and evidence of plasma leakage (≥ 20% increase in the hematocrit from the baseline value). According to WHO, DHF is classified into 4 gradings of severity as presented in Table 2.1.

Table 2.1. Grading of DHF according to WHO

Grade	Clinical Manifestation
1	no shock: only positive tourniquet test
2	no shock : has spontaneous bleeding other than a positive tourniquet test
3	shock
4	profound shock with unmeasurable blood pressure or and / pulse

Reference: Malavige *et al*, 2004

Dengue shock syndrome is the severe form that is characterized by changes in pulse rate and blood pressure with cold extremities and restless. Shock usually occur during or immediately between 3 and 7 days after the fever is down due to plasma leakage and abnormal hemostasis that could render patients unconscious (Guzman and Kouri, 2003).

2.1.2 Etiology of dengue infection

Dengue infection is caused by dengue virus which belongs to *Arthropod Borne Virus* (Arbovirus) of the flavivirus genus of Flaviviridae family. Dengue virus has four serotypes namely DEN1,DEN2, DĖN3, and DEN4. The four dengue serotypes can be distinguished by serological methodologies. The structure of the serotypes antigens is similar to the others, but antibody against each serotype can not give cross protection (McBride and Ohmann, 2000; Shu and Huang, 2004; Noisakran and Perng,2008; Guzman *et al*, 2010). All dengue serotypes can be found in Indonesia whereby serotype DEN3 is dominan and causes severe clinical manifestation (Ministry of Health Indonesia,2005).

Dengue viruses have a ribonucleic acid (RNA) genome that is surrounded by a single chain of nucleotides icosahedral and is enveloped by lipid membrane. The virion has a length of approximately 11 Kb (Kilobases), and consists of a spherical particle, 40-50 nm in diameter, with a lipopolysaccharide envelope. The genome consists of three structural protein molecules that include C(core), prM (membrane), and E (envelope) that form the virus particles and seven nonstructural protein molecules NS1, NS2a, NS2b, NS3, NS4a, NS4b and NS5 (Figure 2.1). Viral protein and RNA synthesis commonly occur in the cytoplasmic of host cells. The NS protein is only found in infected host cells and is required for replication of the virus. The replication begins within 15 hours after infection and does not significantly affect the metabolic function of the host cells (Chuansumrit and Tangnararatchakit, 2006; Noisakran and Perng, 2008; Guzman *et al*., 2010; Whitehorn and Simmons, 2011).

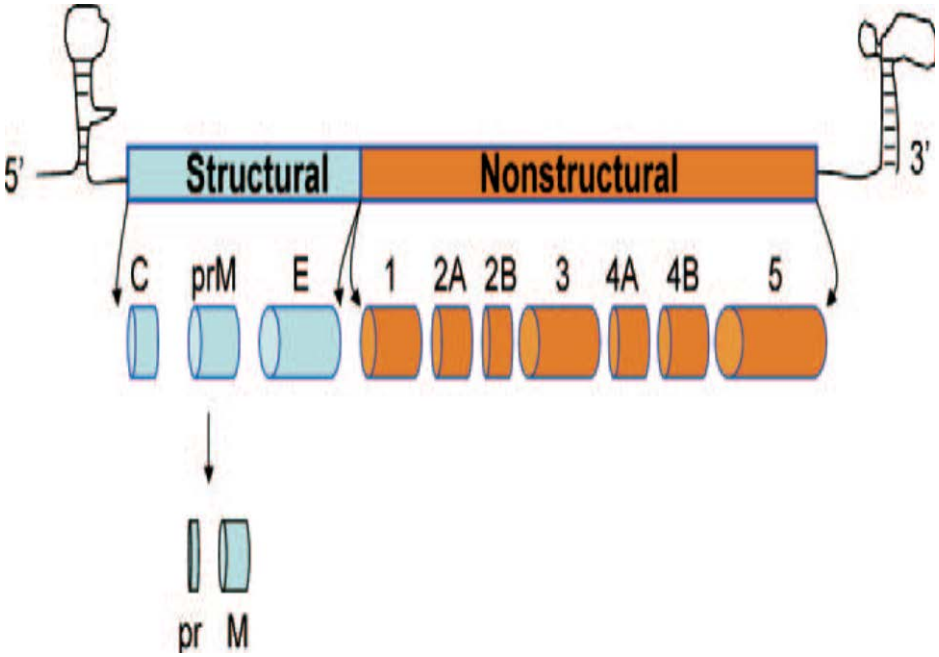

Figure 2.1. The dengue viral genome

A person can be infected with all four serotypes during his / her lifetime. Infection with one serotype of dengue virus produces a lifelong immunity against that specific serotype, but only partial protection is against other serotypes (Shu and Huang, 2004). An infection with a different type increases the risk of complication and the variety in severity depends on the level of virus virulence, viral load and host response (Chuansumrit and Tangnararatchakit, 2006; Wearing and Rohani, 2006; Noisakran and Perng, 2008). The virulence of dengue virus is related to the virus genotype and it plays a role in the pathogenesis of DHF. Dengue virus may infect and replicate in the endothelial and epithelial cells and the dengue virus antigen is detected in cells of the monocyte-macrophage lineage in the lymphoid organs, lung and liver of patients with dengue infection (Mc Bride & Ohmann, 2000).

2.1.3 Transmission

Dengue transmission is a complex phenomenon that involves dengue viruses, the mosquito vectors, human as reservoir and environment which favors the interaction between the mosquito vector and human host. The size, density and biological status of vector mosquito population are critical to the transmission of the dengue virus (Halstead, 2008).

The main vector involved in the spread of dengue fever is *Aedes aegypti*, while the others are *Aedes albopictus* and *Aedes scutellaris*. *Aedes aegypti* is a small, dark mosquito with white marking on its legs and a marking in the form of a lyre on the thorax (Figure 2.2). This mosquito originated in Africa, but now is widespread in tropical and subtropical region throughout the world. Female mosquitoes likes human blood (anthropophilic), while male mosquitoes prefer eating fruits and flowers. These mosquitoes commonly live around human dwelling in and around the house and in urban area (Halstead, 2008).

Figure 2.2. Aedes aegypti mosquito

Aedes aegypti experiences a complete metamorphosis of eggs, larvae, pupae and adult mosquito. During the stage of eggs, larvae and pupae *Aedes* mosquitos live in water. In general, the eggs will hatch into a larvae approximately 2 days after the eggs submerged in water. Larvae stage usually lasts 6-8 days and the pupae stage 2-4 days. Overall growth in eggs into adults mosquito lasts 9-10 days as presented in Figure 2.3 (Ministry of Health Indonesia, 2005).

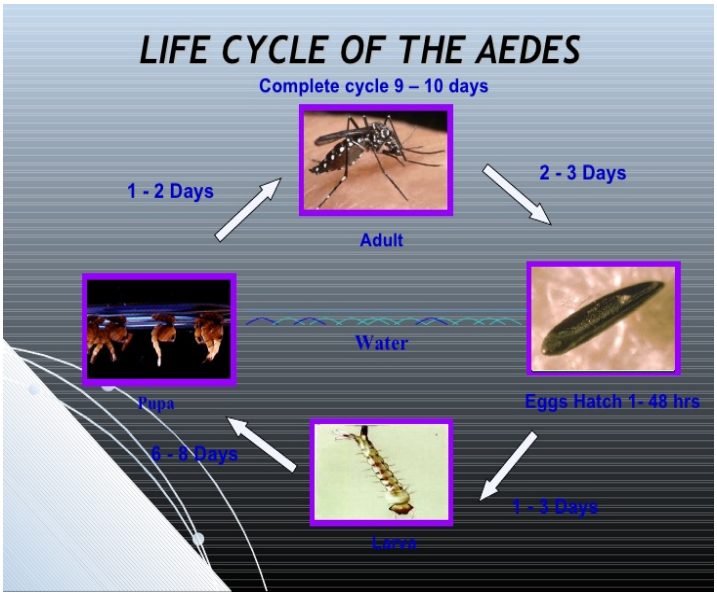

Figure 2.3. Metamorphosis of Aedes aegypti

Female *Aedes* mosquitoes transmit dengue viruses through its characteristics of biters day and preference for human blood. They feed in the morning (9.00 am until 10.am) and late afternoon (4.00 pm until 5.00 pm). *Aedes* mosquito have multiple biting to complete a blood meal so that they are enough for growth and development of eggs. Then the mosquito will rest in a place with optimum condition (humidity

and dark place, and hanging clothes) while waiting for the mosquito eggs to mature (Suyasa *et al.*, 2008). After three days feeding on blood, the mosquito lay their eggs inside a container above the water line. Eggs can survive for six months or more. The breeding places of *Aedes* mosquitoes are dark colored artificial or natural water containers that are not directly related to the ground and commonly located in and around the house and protected from the sun. *Aedes* habitats in urban area vary. However, 90% are man made containers such as water storage container, bathtubs, drums, pails, jars, discarded tins, discarded bottles, flower pots, discarded tyres etc (Halstead, 2008).

Dengue hemorrhagic fever is transmitted by the mosquito *Aedes aegypti*. The female *Aedes aegypti* bite an infected person during the viraemic phase of the disease, and usually lasts 4 to 7 days (Figure 2.4). The virus passes from the mosquito intestinal tract to the salivary glands after an extrinsic incubation period, duration from when a mosquito bites an infected person until it becomes infectious, which takes approximately 8 to 12 days. Dengue virus is transmitted from mosquito to human by mosquito salivary proteins. After intrinsic incubation for 3-14 days (average for 4-6 days) the symptoms of the disease appear such as fever, head ache, myalgia, nausea, vomiting and rash (McBride & Ohmann, 2000; Ministry of Health, 2005; Clyde *et al.*,2006; Guzman *et al.*, 2010).

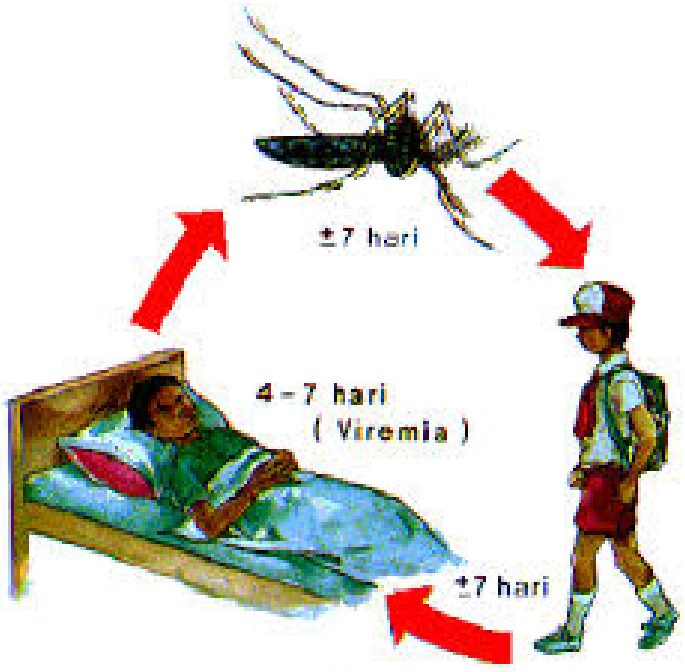

Figure 2.4. Chain of dengue infection

Vector density play a role in the transmission of dengue fever, particularly *Aedes aegypti*. Urbanization in tropical countries has resulted in both the proliferation of *Aedes egypti* and the increasing of susceptible human hosts number. Adult survey, larva survey and egg trap survey were carried out to determine the density of vector mosquitoes. A few indices were used as indicators to determine the abundance of vector mosquitoes such as house, container and breteau indices (Sanchez *et al.*, 2006; Abdalmagid and Alhusein Sh, 2008).

Climatic factors such as temperature and humidity that favor the survival of adult mosquito beyond the extrinsic incubation period, thereby increasing the viral transmission. However, increase transmission also occurs in the rainy season (Mc Bride & Ohmann, 2000).

2.1.4 Epidemiology of DHF

Dengue hemorrhagic fever, one of the most widespread vector borne disease of humans worldwide, initially occurred as epidemic in the tropical and subtropical countries. With increasing globalization and human movement, the geographic expansion of *Aedes aegypti* mosquito vector causes dengue virus infection to occurr worldwide. At the beginning of this new milleneum, approximately 50 to 100 million cases of dengue fever and 500,000 of cases of the DHF occurred annually, predominantly in children under 15 years of age (Gubler, 2002; Guzmán and Kouri, 2003; Guha-Sapir and Schimmer, 2005).

As many as 3.6 billion people are living in areas with high risk of dengue infection with approximately 230 million infection worldwide (Wilder-Smith *et al*, 2012). The majority of cases were in Southeast Asia and the Western Pacific (Guzman *et al*, 2010). World Health Organization (WHO) reported that the annual number of DHF cases for the period 2000-2004 had increased and almost doubled compared to 1990-1999 (Guzman and Kouri, 2003). Now, Dengue is endemic in many countries in Southeast Asia, and a public health problem in Indonesia, Myanmar, Sri Lanka and Thailand (Ministry of Health Indonesia, 2010). Likewise in Malaysia and Singapore (Carrasco *et al*, 2011).

In some tropical and subtropical regions the number of DHF cases are increasing and became a significant cause of death. In Indonesia dengue outbreak occur annually in several provinces with the largest occured in 1998 and 2004 with 79,480 cases and over 800 people died (Kusriastuti and Sutomo, 2005).

Although DHF may infect everyone, however children were more common to have DHF than elderly. It could be related to immunity and susceptibility to dengue fever. On the other hand, the risk of dengue infection in female is equal to male (Guha-Sapir and Schimmer, 2005).

2.1.5 Factors associated with DHF

Factors that are responsible for DHF incidence are complex and not fully understood. However some factors such as the increase in population density and unplanned urbanization, inadequate water supply and waste management system, the increase in air travel, the lack of effective vector control program , the climatic change and poor sosio-economic status have been identified as the key determinants (Guzman and Kouri, 2003; Torres and Castro, 2007).

Several studies had been conducted to look into factors that contributed to DHF incidence. A study conducted by Siquera *et al* (2004) found that older age, low education, and low income population were significantly associated with dengue fever. This was further supported by a study by de Maltos Almeida *et al* (2007) reported that the risks of contracting DHF were similar to the previous study and were associated with socioeconomic, demographic and infrastructure characteristics and higher household density.

A study conducted by Phuong *et al* (2008) found that the farming occupation, number of children less than 15 years old in household, inexperience with dengue

fever in household, garden near the house and water containers having mosquito larvae were associated with a higher risk of dengue fever in Vietnam.

Other factors that contributed to increase DHF incidence were poor sanitation, housing pattern, poverty, illiteracy, cultural practices and climate (temperature, rainfall, humidity). All these factors were noted to promote vector proliferation (Chao *et al.*, 2000; Hossain *et al.*, 2000; de Mattos Almeida *et al.*, 2007).

Sosio-economic factors also play role in the incidence and prevalence of DHF. These factors are known to affect the abundance of *Aedes aegypti* mosquitoes and disease transmission related to housing with unhygienic condition and poor household design. Housing with the presence of solid waste around the house and prolonged storage of water for domestic use created potential breeding habitat for *Aedes aegypti*, therefore increasing the transmission of dengue infection (Nagao *et al.*, 2003; Mondini and Chiaravalloti Neto, 2007). A study by Heukelbach *et al* (2001) in Fortaleza found that there was no association between socioeconomic factors and dengue fever. The same was reported by Mondini *et al* (2007) in Southern Brazil where they found no association between risk occurence of dengue and socioeconomic factors. While Mobarak study *et al* (2008) in Dhaka city found dengue fever more commonly in middle and high sosioeconomic group.

A study conducted by Bohra and Andrianasolo (2001) in Rajasthan India investigated the association between risk of dengue and sosiocultural factor and they found housing pattern, limited use of mosquito protection measures, irregular water