Course	Health Innovation	Name	Miho Inokuchi
Thesis Title	Association between Dengue severity and plasma levels of Dengue-specific IgE and Chymase		

Abstract of Master's Thesis

Background/Objectives: Dengue disease has been expanding throughout the globe making 390 million people its victims making it a major public health problem with substantial social and economic burden for years now. Despite remarkable efforts have been made in dengue virus (DENV) research, there is still a huge knowledge gap particular in the pathogenesis, clinical research and case management. Recent studies suggest that mast cell mediators such as immunoglobulins (IgE) and chymase have potential roles in dengue severity, however, kinetics of these factors in the course of dengue infection are not well investigated, so we attempted to uncover it in this study.

Materials and methods: This was a hospital-based prospective study conducted at Nguyen Dinh Chieu Hospital in Vietnam from 2009 to 2014. We enrolled a total of 85 OFI (other febrile illness) and 111 dengue patients (all age and sex) confirmed by detecting plasma levels of specific antibody and viral RNA using enzyme linked immuno-sorbent assays (ELISAs) and reverse transcription polymerase chain reaction (RTPCR). Blood samples were collected from each patient every day before and after the shock or defervescence and at post-discharge. The patients were classified as Level 1, Level 2, and Level 3 based on clinical intervention they received. Plasma samples collected at multiple time points were subjected to measurement of plasma chymase levels, and total IgE by conventional ELISA; and DENV-specific IgE by in house developed IgE capture ELISA; and the latter was developed in-house as IgE capture ELISA. Kinetic profiles of DENV-specific IgE, total IgE, their ratios (S/T ratios), and chymase levels were resolved for all 3 levels of dengue severity.

Results: Kinetic profiles of DENV-specific IgE, total IgE, S/T ratios, and chymase were drawn for each level of dengue severity. The DENV-specific IgE kinetics showed an increasing trend with the course of illness and remained high at post-discharge although no significant difference between different severity levels was observed. We did not find any notable trend in the kinetics of total IgE with any severity. However, when we focused on the S/T ratio, its kinetics resembled the increasing trend of DENV-specific IgE and most serious Level 3 patients group remained the highest throughout the sourse of illness. Moreover, the S/T ratio of early acute phase samples (-48 to -6 h before shock or defervescence) from patients different levels of dengue severity and OFI revealed a trend of increasing S/T ratio with the increasing severity (OFI < Level 1 < Level 2 < Level 3) and that the S/T ration showed statistically significant

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difference between Level 3 and Level 1, and Level 3 and OFI. As an early predictor of dengue severity to identify Level 3 patients among total dengue patients, S/T ratio achieved a sensitivity of 88% and specificity of 68%.

Conclusions: We described the precise kinetics of total IgE, DENV-specific IgE, S/T ratio and plasma chymase in different severity levels of dengue. On top of it, S/T ratio was found to be associated with dengue severity and it could be a potential candidate for the early predictor of dengue severity.

∗   The abstract, containing the objective, method, result and conclusion should not exceed c.1000 words (300-500words/page, double sided on A4 paper)