Abstract of Master's Dissertation

No.1

Course	Health Innovation Course	Name	Nguyen Thi Ngoc Phuong
Thesis Title	Verification of candidate biomarkers to early predict severe dengue		

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Objective:

Dengue is one of the most concerned mosquito-borne viral diseases of the tropical and subtropical countries caused by dengue virus. Dengue has a wide spectrum of illness ranging from asymptomatic to potentially life-threatening conditions known as severe dengue (SD). SD is the major cause of mortality among dengue-infected patients, and only a small proportion progress to such severe forms. However, due to the lack of reliable predictors of severity, huge number of patients are hospitalized based on warning signs. Early prediction of severity not only reduces the hospital burden but also contributes to the quality care for patients at risk of SD. As of now, no routine prognostic tests are available to predict severity and outcome of dengue. Therefore, the present study aimed to verify the association of circulating cfDNA and seven plasma proteins (earlier identified by proteomic approach during the discovery phase - TGFBIp, antithrombin III, transferrin, ceruloplasmin, fetuin-A, SPTLC-3, and otopetrin-3) with dengue severity and explore the prognostic values of promising candidates for early prediction of SD.

Method:

A total of 111 laboratory-confirmed dengue patients and 85 OFI cases were enrolled in a hospital-based prospective study conducted at Nguyen Dinh Chieu Hospital, Vietnam from July 2011 to May 2013. Dengue patients were classified into different severity levels (level I, level II and level III) based on the clinical intervention they received. The acute-phase plasma samples were subjected to PicoGreen assay to measure the level of cfDNA, and protein specific quantitative ELISAs to estimate plasma levels of seven proteins of interest. The significant difference in concentrations of cfDNA and the plasma proteins among different severity levels of dengue, and between each level with OFI were analyzed. Receiver-operator characteristic (ROC) curve was also generated to determine the discriminatory performance of the potential biomarkers in identifying the most severe level III patients.

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

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Result:

The results showed that plasma cfDNA levels in acute phase of level III dengue patients were significantly higher as compared to that of level I + II (p = 0.038). The ROC curve analysis indicated an acceptable discriminatory value of cfDNA with an AUC of 0.74 (95% CI, 0.56 - 0.91; p = 0.039), and a cut-off of > 36.85 ng/mL was able to identify level III cases from other dengue infected-patients with a good sensitivity of 87.5% (95% CI, 47.4% - 99.7%) and specificity of 55.6% (95% CI, 38.1% - 72.06%). Among seven verified proteins, TGFBIp was found to be significantly elevated in level II patients compared to level I (p = 0.014), level III (p = 0.025) and OFI (p = 0.003) during early phase of illness. However, the rest 6 plasma proteins did not show significant difference among different levels of dengue severity.

Conclusion:

We found a significant association of acute-phase cfDNA levels with dengue severity which could be a potential biomarker for early prediction of severe cases. Additionally, TGFBIp levels could also be used as a good indicator to early discriminate level II dengue patients from level III, and it requires further evaluation.

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