IS-AC-3-3 Prediction of pre-eclampsia and its severity by soluble FMS-like Tyrosine Kinase 1 and Placental growth factor

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[Objective] Pre-eclampsia (PE) presents the greatest risk to the mother and her fetus with challenges in early diagnosis or prediction of PE and its severity. There is no reliable test for its prediction. It has been demonstrated that biomarkers ; soluble fms -like tyrosine kinase-1 (sFlt-1) and placental growth factor (PIGF) seem to play a critical role in the prediction of PE. The serum level of sFlt-1 is increased, PIGF concentration is decreased and sFlt-1/PIGF ratio is raised in women who will develop PE. The aim of this study was to evaluate the role of sFlt-1, PlGF and sFlt-1/PlGF ratio in prediction of PE and its severity. [Method] The study design is nested case control study. The study was carried out from January, 2013 to December, 2013 in Central Women's Hospital (CWH), Yangon and Insein General Hospital (IGH). The study population was 987 non PE primigravid women who were selected from the antenatal (AN) clinics at gestational age between 21 and 32 weeks. Blood was taken at the first appointment and serum samples were stored until testing. Clinical data including demographic information, risk factors for PE, blood pressure, proteinuria, and signs and symptoms of severe PE were recorded. The participants were followed up until postpartum 6 weeks. Fifty patients who developed PE were represented as 'cases'. Each woman with PE was matched according to maternal age and gestational age at blood sampling to one pregnant woman without PE. They were represented as 'control'. The levels of sFlt-1 and PlGF of total 50 pairs of cases and controls were analyzed using Enzyme Linked Immunosorbent Assay (ELISA). [Result] The marked increase in sFlt-1 concentration and sFlt-1/PlGF ratio before the onset of PE, accompanied by decrease in PlGF levels were detected in this study. In prediction of PE, there were antenatal sFlt-1 cutoff value 500pg/ml with sensitivity 74% and specificity 82% ; and sFlt-1/PlGF ratio cutoff value 3.6 with sensitivity 74% and specificity 82%. However, cutoff value of PlGF for prediction of PE was not valid because the Receiver Operator Characteristic (ROC) curve crossed the diagonal line. It has limited usefulness. For prediction of severe PE, there were sFlt-1 cutoff value 1275.75 pg/ml with sensitivity 91% and specificity 87% ; PlGF cutoff value 110pg/ml with sensitivity 91% and specificity 97% ; and sFlt-1/PlGF ratio cutoff value 14.79 with sensitivity 91% and specificity 97%. [Conclusion] This study demonstrated the marked increase in the sFlt-1 and sFlt-1/PlGF ratio with decreased PlGF with statistically significant results in predicting PE and severe PE. These findings supported the hypothesis of predicting the occurrence of PE and severe PE. Further prospective, longitudinal studies on larger number of women in which serial measurement of sFlt-1, PlGF and their ratio throughout pregnancy are needed for better assessment of the relevance of these biomarkers to predict PE and its severity. Prediction of women at risk of developing PE and severe PE will contribute to prevention, early diagnosis and treatment leading to reduction of maternal and perinatal morbidity and mortality.

IS-AC-3-4 Preeclampsia (PE) serum disrupts the autophagy/lysosome pathway cooperated with endoplasmic reticulum (ER) stress

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[Objective] We have reported that impaired autophagy contributes to the shallow trophoblast invasion and poor vascular remodeling (1st step of PE). The aim of this study is to clarify the correlation between autophagy and dysfunction of placenta (2nd step of PE). [Methods] We used placental tissues and serums from PE patients with informed consent. Proteostat dye® is used for detecting aggregated proteins. [Results] We firstly found that the number of lysosome was significantly decreased ($p=0.037$), and aggregated proteins were increased ($p=0.021$) in the syncytiotrophoblast in PE placenta. Secondarily, ER stress inducers inhibited the lysosomal number and functions in a trophoblast cell line, suggesting that ER stress reduces autophagy and protein quality control. We then took notice of transcriptional factor EB (TFEB), a master regulator of autophagy and lysosome biogenesis. The expression of TFEB was significantly decreased ($p=0.005$) in the PE placenta than that in normal placenta. Finally, serum from PE patients suppressed the TFEB activation via hyper-activating mammalian target of rapamycin. [Conclusion] ER stress as well as PE serum cooperatively impaired homeostasis in PE placenta via suppressing autophagy and lysosome functions. As overexpression of TFEB is known to improve some neurodegenerative disease in mice model, TFEB activation would be a new therapeutic option for PE.