

# Pre-eclampsia is more than a vascular disease

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## **CHAPTER 7**

### Valorisation

## PRE- ECLAMPSIA IS MORE THAN A VASCULAR DISEASE

The studies reported in the present thesis underline the importance of several markers and genetic aspects that evidence key issues in the pathogenesis of pre- eclampsia (PE) which could in the near future serve as predictors of the development of the disease.

## RELEVANCE

Approximately 5 to 14% of all pregnancies may be complicated with PE. It is a serious issue occurring during women's reproductive years. Despite attempts at prevention or intervention it is still a leading cause of maternal and fetal morbidity and mortality in both developed and non developed countries. There is no treatment for this disorder other than the termination of pregnancy which increases the rate of iatrogenic preterm births. Much research in the past has mainly focused on epidemiological, clinical and preventive aspects; today biochemical and molecular aspects seem to gain relevance as once we identify who will develop PE, intervention can be instated early, and although cure might not be feasible, at least its negative impact can be ameliorated. Although there have been advances in prenatal and neonatal care, prediction of PE is still shadowed by the lack of a unique predictive biochemical or molecular marker which could: a) allow its early detection and management and b) aid in the selection of appropriate candidates for new therapeutical approaches.

## INNOVATION

Currently, the cause of PE is unknown; however, what we do know is that early diagnosis of PE improves maternal and fetal outcome. This thesis provides important insights to the understanding of several pathogenic pathways in the development of PE. PE in Latin America is a serious problem as it causes not only increased maternal fetal morbidity and mortality yet it imposes an important and significant burden to the healthcare system. Poverty conditions observed in Latin America together with inadequate prenatal care seem to increase the negative impact that PE has over female health and the healthcare system. Despite the limitations of the poverty conditions found in our country the present thesis sought at providing important insights in the search of a unique or various cost effective markers required for the screening and early detection and intervention of the problem of women of any socio-economic condition. In this sense, this thesis is innovative in its conception, first because it provides evidence that endothelial dysfunction is also present in the fetal circulation. Such data is still scarce or non existent. Second, it provides insights on various markers that evidence several pathogenic pathways of PE, highlighting the effect of altitude of residency in

terms of NO and CoQ<sub>10</sub> levels. The studied markers can be eventually validated in the near future for the early screening of PE. In this sense, the data presented in Chapter 2 regarding sFlt-1 and its higher levels found in PE women in 2009 definitively have lead others to study and validate this marker as a first trimester PE screening analyte together with other biochemical (i.e. placental growth factor, beta-HCG, alpha-fetoprotein, inhibin) and biophysical (i.e. uterine artery resistance o pulsatility index) aspects. This speaks about the originality of the contribution of our data, and despite eventual limitations our approach provides the basis for future novel investigation.

## **ACTIVITIES/PRODUCTS**

Despite the fact that the biochemical markers and genetics aspects reported in this investigation seem promising in the prediction of PE, issues still remain to be elucidated. Although sFlt-1 seems a promising predictive marker it still needs to be combined with other biochemical and physical aspects, therefore there is still an urgent need of finding a unique marker that can not only predict the disease yet define the one abnormality that is the cause of the disease and not the effect. The author would also like to highlight the important role that genetics and epigenetics may have in elucidating the cause of the disease. Future research should focus in the correlation between genetic abnormalities or phenotypes encountered in women with PE with biochemical abnormalities and clinical stages or outcome of the disease.

## **SCHEDULE AND IMPLEMENTATION**

Further perspectives for the utility of the studied biochemical markers, especially sFlt-1 and genetic aspects seem not only promising yet intriguing. Indeed, the possibility to validate the effectiveness of an innovative novel therapeutical approach for PE based on biochemical and genetic markers instead of clinical criteria seems a major hot topic for the near future. Our data provides insights that seem to aid this promising perspective.