ABSTRACT

Early and late onset preeclampsia are being increasingly recognized as two different subclasses of the disease having different etiologies and therefore, a different clinical expression. It is well accepted that oxidative stress plays a major role in the pathogenesis of preeclampsia. However, extensive studies investigating the pro- and antioxidant status of both the subclasses are lacking. All pre-eclamptic women included in this study were associated with excessive oxidative stress; however, women with early-onset preeclampsia appeared to be more severely affected. Oxidative damage to lipids, proteins and DNA also showed a similar trend with the early onset cases being affected to a greater degree. It was also observed that reactive oxygen species were more effective in causing oxidative deterioration of lipids and DNA than at modifying proteins. On analyzing the placental tissue lysates, in contrast to late onset preeclampsia, early onset cases were characterized by enhanced placentation abnormalities and systemic endothelial damage, as evidenced by increased apoptosis. Perturbations in inflammatory response mediated by excessive reactive oxygen species generation are well established. Significantly higher levels of pro-inflammatory cytokines were observed in early onset preeclampsia women. These cytokines in turn, induced oxidative stress and caused alterations in the secretion of vasodilators and angiogenic growth factors. Significant alterations in extra cellular matrix remodeling in early onset preeclampsia are a result of an active association between oxidative stress and the matrix metalloproteinases (MMPs) system. A gross imbalance between MMPs and their inhibitors in early onset preeclampsia indicates poor extra cellular matrix remodeling in this group. Metabolites including specific lipids and amino acids at a cellular level were also found to be differently expressed in early onset preeclampsia. Summarizing, the findings of the present thesis indicate that early and late onset preeclampsia may be treated as two separate disease entities since excessive systemic endothelial dysfunction appears to be a a central feature of early onset preeclampsia. This observation is expected to help in improved diagnosis, treatment, and management of preeclamptic patients.

Key words: Early onset preeclampsia, late onset preeclampsia, oxidative stress, reactive oxygen species, extra cellular matrix remodeling, matrix metalloproteinases, cytokines, cellular adhesion molecules, metabolite profiling

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