Genetic study shows that the risk of pre-eclampsia is related to blood pressure and BMI

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Pre-eclampsia, usually diagnosed by increased blood pressure and protein in urine, affects up to 5% of pregnant women. It contributes

worldwide to the death of estimated 50000 women and up to one million babies annually. The condition is also associated with an increased risk of cardiovascular diseases among mothers and their children later in life. There is an inherited risk, with women with a family history of pre-eclampsia at greater risk of developing the condition themselves.

In the InterPregGen study, researchers from the UK, Iceland, Finland, Norway, Denmark, Kazakhstan and Uzbekistan studied how maternal genetic variation influences the risk of pre-eclampsia. The team studied the genetic make-up of 9,515 pre-eclamptic women and 157,719 control individuals.

The results, reported today in *Nature Communications*, pinpointed DNA variants in the ZNF831 and FTO genes as risk factors for pre-eclampsia. These genes have previously been associated with blood pressure, and the FTO variant also with body mass index. Further analysis revealed other blood pressure related variants in the MECOM, FGF5 and SH2B3 genes also associating with pre-eclampsia. These variants increase the risk of pre-eclampsia by 10-15%.

The study also shows that overall genetic predisposition to hypertension is a major risk factor for preeclampsia and thus a large number of variants each with a small effect may also contribute to the risk. These current results complement the earlier findings of the same researchers, who showed that a variant near FLT1 gene in the fetal genome affects mothers' risk of developing pre-eclampsia.

The genes identified so far fit hand-in-glove with other current knowledge of pre-eclampsia as hypertension and obesity are known maternal risk factors. This study shows that these associations are partly explained by inherited predispositions. However, they only explain a part of the pre-eclampsia risk. Whether the remaining unidentified factors act through the maternal or fetal genome, or both, remains to be seen.

The new insights from this study could form the basis for more effective prevention and treatment of pre-eclampsia in the future, and improve the outcome of pregnancy for mother and child.

The five-year study was coordinated by Dr. Linda Morgan from the University of Nottingham's School of Life Sciences; Nottingham Professors Emeritus Noor Kalsheker (Clinical Chemistry) and Fiona Broughton Pipkin (Obstetrics and Gynecology) were among the collaborators.

Professor Fiona Broughton Pipkin said: "The new insights from this study could form the basis for more effective prevention and treatment of pre-eclampsia in the future, and improve the outcome of pregnancy for mother and child."

"They could also encourage GPs to follow-up more closely women who have had pre-eclampsia."

More information: undefined undefined et al. Genetic predisposition to hypertension is associated with preeclampsia in European and Central Asian women, *Nature Communications* (2020). DOI: 10.1038/s41467-020-19733-6

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