

Novel information about the effects of in vitro fertilization on embryonic growth

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It is known that in vitro fertilization (IVF) can affect the size of the newborns. Children derived from fresh embryo transfer have smaller birth weight, and surprisingly, children derived from frozen embryo transfer have subtly higher birth weight in average.

In the study conducted by University of Helsinki, Helsinki University Hospital and University of Tartu, the researchers looked for mechanisms how the IVF can alter the embryonic growth. More than three percent of newborns are derived from IVF treatments currently in Finland.

86 couples with IVF derived pregnancies and 157 couples with spontaneous pregnancies as controls were recruited for this study. IVF samples were divided in two groups depending on whether the embryos were transferred in utero fresh after fertilization, or after they were frozen and thawed before the <u>transfer</u>.

The regulation region of two growth genes, insulin-like growth factor 2 and H19 was examined. A <u>common genetic variation</u> in this region has been associated with different amount of epigenetic marks depending on which variants an individual has inherited from the parents.

DNA methylation, the most well-known epigenetic mark was investigated in this study. These methyl groups bind to the DNA strand and affect the gene function.

"We divided the placentas in genotypes according to the variants which



the newborns had inherited, and we observed that the effect of IVF on the <u>epigenetic marks</u> depends on the genotype." explains Adjunct professor Nina Kaminen-Ahola, the leader of the research team at the University of Helsinki.

Furthermore, the <u>birth weight</u> and placental weight as well as the head circumference of newborns, which were derived from fresh <u>embryo</u> <u>transfer</u>, were smaller only in one particular genotype. Also, the newborns with this genotype, who were derived from <u>frozen embryo</u> <u>transfer</u>, were significantly heavier.

"This work together with our previous work about the effects of prenatal alcohol exposure on embryonic development, reveals a genotype-specific effects of environmental factors." states Kaminen-Ahola. "As far as I know, this is the first genetic factor which has been associated with the phenotype of IVF-derived <u>newborns</u>".

"This single nucleotide polymorphism locates in the binding site of a regulatory protein, and thus could affect the binding of the protein as well as gene function in altered environmental conditions. However, the effect of this variation on the regulation of these growth genes should be examined by functional studies."

Kaminen-Ahola emphasizes that these changes are not dangerous and IVF treatments are safe. "Low birth <u>weight</u> has been associated with increased risk for heart and vascular diseases and therefore it is necessary to understand the mechanisms underlying it to develop the IVF methods".

"In the future, this could be a part of personalized medicine and help to target the sources of health care system more specifically."

More information: Heidi Marjonen et al, rs10732516 polymorphism



at the IGF2/H19 locus associates with genotype-specific effects on placental DNA methylation and birth weight of newborns conceived by assisted reproductive technology, *Clinical Epigenetics* (2018). DOI: 10.1186/s13148-018-0511-2

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