

# Abstract

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## Effect of B vitamins and genetics on success of in-vitro fertilisation: prospective cohort study.

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**BACKGROUND:** There is a need to understand what affects the success of in-vitro fertilisation (IVF) and the rate of resulting twin births so that pregnancy rates can be improved and multiple gestations avoided. Our aim was to assess the role of B vitamins and genetics.

**METHODS:** We did a prospective cohort study of 602 women undergoing fertility treatment. We assessed intake of folate and vitamin B12 with a questionnaire and measured their plasma and red-blood-cell concentrations by radioimmunoassay. We measured five B-vitamin-related gene variants in women who received treatment and in 932 women who conceived naturally.

**FINDINGS:** The likelihood of a twin birth after IVF rose with increased concentrations of plasma folate (1.52, 1.01-2.28;  $p=0.032$ ) and red-cell folate (1.28, 1.00-1.65;  $p=0.039$ ). There was no association between folate and vitamin B12 levels and likelihood of a successful pregnancy. Women homozygous for the 1298 CC variant of methylenetetrahydro-folate reductase (MTHFR), rather than the AA variant, were less likely to produce a livebirth after IVF (0.24, 0.08-0.71;  $p=0.003$ ) or to have had a previous pregnancy (0.42, 0.21-0.81;  $p=0.008$ ).

**INTERPRETATION:** Our findings suggest that MTHFR genotype is linked to a woman's potential to produce healthy embryos (possibly through interaction with genes related to DNA methylation). In women likely to have a successful IVF pregnancy, high folate status increases the likelihood of twin birth after multiple embryo transfer. Proposals to fortify the UK diet with folic acid could lead to an increase in the number of twins born after IVF.

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