

Is There a Genetic Component to Hyperemesis Gravidarum?

Nausea and vomiting are common in pregnancy affecting between 50 and 85% of women. Hyperemesis gravidarum (HG), however, represents the severe end of the spectrum where nausea and vomiting result in dehydration, metabolic alkalosis and weight loss necessitating hospital admission and intravenous rehydration and in more severe cases, parenteral or nasogastric feeding. It is estimated to complicate approximately 0.5% of pregnancies but there is geographical and racial variation in incidence. These differences may, however, reflect reporting mechanisms and criteria for hospital admission in different studies.

Generally, the condition is not associated with adverse fetal outcome. There is no evidence of an increase in birth defects whether or not anti-emetics are taken by the mother and nausea and vomiting in early pregnancy is associated with a reduced risk of miscarriage. Likewise, there is no difference in birth weight and gestational age at delivery for women with HG once the hyperemesis resolves and there is a 'catch up' to the normal total pregnancy weight gain. If weight loss is severe with no catch up, there is an increased risk of low birth weight. For the mother the consequences of HG can be serious with prolonged hospitalisation with loss of work and family contact. Serious maternal morbidity is rare now because of intravenous rehydration, vitamin and mineral supplementation and parenteral feeding.

Treatment is otherwise challenging. Intravenous fluid usually requires hospital admission although there are newer outpatient models of care that are proving to be effective. The fear of teratogenicity and limited efficacy limits anti-emetic therapy. Pyridoxine (Vitamin B6) reduces nausea (but not vomiting) and there are equivocal results to support the benefit of P6 acupuncture and ginger. In severe HG, thiamine (Vitamin B1) should be administered to prevent rare complications such as Wernicke's encephalopathy. The pathophysiology of the condition is poorly understood. There is a positive correlation with B-HCG levels. Early pregnancy failure is less likely with hyperemesis gravidarum and HG is more likely to occur in association with multiple and molar pregnancy. Smokers are less likely to have HG. It was hypothesised that HG was a conversion disorder where psychological distress transformed into physical symptoms but there is little evidence of this from studies. However, there are suggestions that psychological responses to the physiologic condition may become entrenched or conditioned and as such psychological therapy, such as hypnosis, may have some benefit.

More recently, the hypothesis that HG may have a genetic aetiology has been explored. Siblings and mothers of affected individuals are more likely to have HG themselves but it unclear what role environmental factors play in this. There is one study that showed that the concordance rate in twins was twice as high for identical than non-identical twins. In an attempt to further explore the role of nature versus nurture in HG Vikanes et al recently examined the incidence of HG in the offspring of women who had HG themselves. The medical birth registry of Norway provided linked generational data. In a population based cohort from 1967 to 2006, they identified 3704 women and 2290 men whose mothers had had HG. They found that HG was three times more common in women whose mother had HG (3%) compared to the partners of men whose mother had HG (1.18%) OR 2.90. The incidence in the latter group was not different from the incidence in women whose mothers did not have HG (1.1%). They also showed that the risk of recurrence in daughters was increased three fold even if their mother did not have HG in their pregnancy but was affected by HG in another pregnancy. The study was not controlled for other variables such as ethnicity, body mass index, cigarette smoking etc. but the data was based on mandatory reporting of a standardised dataset. The findings support the concept that maternal genotype influences the risk of HG.

There is some evidence that fetal genotype may also influence HG. In some studies, it is reported to be more common in male than female fetuses. Various studies from the Norwegian birth registry help us understand the role and contribution of fetal and maternal genotype. A woman with HG has a 15% risk of the condition recurring in a subsequent pregnancy, a risk that is reduced to 10.9% if her partner changes. The risk of HG is not increased by consanguinity and therefore a recessive fetal gene does not play a major role. This recent study supports a role for the maternal genotype but it does not allow us to control for potential environmental confounders such as diet, behavioural patterns etc. that may pass along the maternal line. However, previous consanguinity studies also support a genetic role because HG is more common in monozygotic than dizygotic female twins. Targetting families with a history of recurrent severe HG may further improve our understanding of this complex disease but in the absence of any understanding of the pathophysiological mechanisms we do not have a candidate gene or group of genes to target. This study will, however, provide solace to many women who suffer or have suffered from this condition and have worried that it is purely a psychological disorder.

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