Iron deficiency anaemia in early pregnancy increases risk of heart defects, suggests new research

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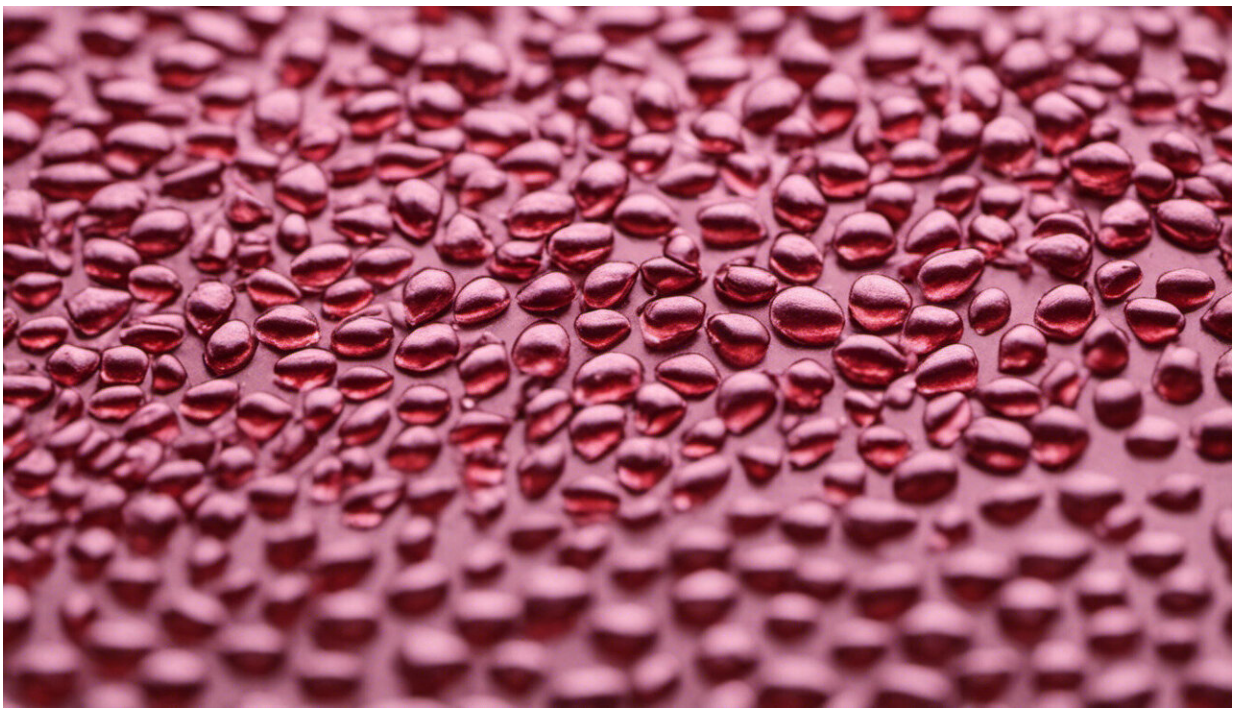

Credit: AI-generated image (disclaimer)

In animal models, iron deficient mothers had a greatly increased risk of having offspring with congenital heart disease (CHD).

A team of University of Oxford researchers, funded by the British Heart

Foundation, have identified an entirely new risk factor for congenital heart disease (CHD). Using an animal model system, researchers have shown that if the mother is severely iron deficient and anemic during early pregnancy, this greatly increases the risk that her offspring will have heart defects.

CHD is the most common human birth defect, affecting 12 babies born each day in the UK. Babies with CHD are born with one or more structural defects caused when the heart does not develop properly in the womb. It is a major cause of infant mortality and requires ongoing medical treatment throughout life. Yet, despite the prevalence of the condition, we do not always know why it happens.

CHD can be caused by a genetic fault inherited from one or both parents, such as a gene mutation. Yet, while more than 100 genes have been associated with individual cases of disease, mutations in these genes can only explain around one-third of cases. The cause of CHD in the other two-thirds of cases is often unknown. In many of these unknown cases, CHD is most likely caused by the embryo being exposed to an abnormal environment in the womb during early pregnancy. However, CHD is not routinely detected until after 20 weeks in pregnancy, so it has long been difficult to collect data on the mother's physiology in the first trimester to establish new risk factors for birth defects.

Duncan Sparrow, Associate Professor at the University of Oxford, BHF Senior Research Fellow and lead researcher on the study said, "Severe maternal iron deficiency in the second and third trimesters is well known to increase the risk of having a low-birth-weight baby and a premature delivery. However, we are specifically looking for the first time at maternal iron deficiency in the first trimester, and we show in mice that maternal iron deficiency can cause severe cardiovascular defects in her offspring."

This finding is supported by a 2020 epidemiological study in China that suggests the risk of having a child with CHD could be increased up to three-fold in women who have low iron intake during early pregnancy.

Professor Sparrow said, "Anemia is a major global health problem, affecting 20-40% of women of child-bearing age, a total of more than 500 million individuals, and half of these are due to iron deficiency. Thus, if our results are applicable to humans, then this may explain why congenital heart disease is relatively common around the world."

The research also showed that the risk of CHD can be greatly reduced if the mother is given iron supplements, provided this happens very early in pregnancy before the heart has formed in the embryo.

According to Dr. Jacinta Kalisch-Smith, first author on the paper, "In humans, the heart forms between weeks 3-9. Our results from the animal study suggest that iron supplementation should probably be given before week 3 to be effective. Even better to take supplements while trying to conceive as women may not know they are pregnant at such an early stage.

"This adds more evidence supporting the WHO's global health priority of making sure that women of child-bearing age are not iron deficient. In fact, WHO recommends that supplementation should begin as early as possible and continue throughout pregnancy."

Dr. Sonya Babu-Narayan, Associate Medical Director at the British Heart Foundation, said, "Congenital heart disease remains the most common birth defect though we don't always know why congenital heart conditions develop. In this research study maternal iron deficiency caused severe congenital heart defects in mice offspring, but if treated the baby's heart developed normally.

"Iron supplementation is a low-cost, safe treatment for women with low iron levels and this research suggests it may have significant benefits for a baby's heart health if taken early in pregnancy when the baby's heart is forming."

The team also investigated the impact of genetic factors when combined with maternal iron deficiency. Around half of people with the genetic condition Down Syndrome have congenital heart disease. A chromosomal abnormality is known to cause the development of CHD in these cases. The team hypothesized that this genetic change in combination with the environmental factor of iron deficiency may increase the likelihood of CHD. Their results showed strong evidence that mouse embryos with a chromosomal duplication modeling Down Syndrome are particularly vulnerable to the effects of maternal iron deficiency, leading to a higher risk of developing severe heart defects in the womb.

The research team hope their findings can be translated to clinical practice to ultimately reduce the birth prevalence of CHD worldwide 'in a manner similar to the impact of folate supplementation that has reduced the birth prevalence of neural tube defects by more than 60% over the past 30 years."

Provided by University of Oxford

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