Severe respiratory infections linked to some congenital cardiovascular defects

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Experiencing severe respiratory infections during the first trimester of pregnancy triples the risk of some cardiovascular defects at birth, a UNSW Sydney study has found.

Maternal infections during pregnancy can have serious implications for babies, including the development of congenital anomalies (also called congenital defects). These are anomalies in the body's structure or function that are present at birth, for example Down syndrome and neural tube defects, which can have lifelong impacts.

Some infections, often referred to as TORCH (Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus (CMV), and Herpes virus), are known to cause congenital anomalies. However, there have been conflicting findings about the impact of acute respiratory infections, for example, influenza.

New research from UNSW, published in *BMC Pregnancy and Childbirth*, shows severe respiratory infections during the first trimester are associated with higher risk of some heart defects.

"There is limited evidence around this issue," said lead author Dr. Abrar Chughtai, from UNSW Medicine & Health. "But our study supports that there is an association between severe respiratory infections during pregnancy and selected cardiovascular anomalies in babies."

Analyzing 1.5 million NSW births

In previous studies, the link between respiratory infections and congenital anomalies has been difficult to prove. The studies often involved asking new mothers, whose babies were healthy or had congenital issues, whether they had experienced a respiratory infection when pregnant.

"The strength of our study is that we used hospital records only and didn't rely on participants' memory," Dr. Chughtai said.

The researchers analyzed data from almost 1.5 million births in NSW

from 2001–2016, linking health records for mothers and babies. The health data included hospital admissions during pregnancy for severe respiratory infections, births, and congenital issues.

Controlling for other factors like age, smoking and other illnesses, the researchers analyzed the association between respiratory infections during pregnancy and various congenital abnormalities.

Increased risk of cardiac defects

The researchers found that there was a link between severe respiratory infections and some types of cardiovascular abnormalities. For the 1,547 mothers who were hospitalized for respiratory infections during the first trimester of pregnancy, seven (0.45%) had babies with these heart and circulation issues. Whereas for the other 1,441,327 mothers in the study, 1,724 (0.12%) had babies with these cardiovascular abnormalities.

"After controlling for other factors, still respiratory infections were associated with selected cardiovascular defects," Dr. Chughtai said.

"The risk is three times higher if the mother had an infection during the first trimester of pregnancy."

Rates of selected major cardiovascular anomalies were also higher in babies if the mother had influenza during the first trimester of pregnancy, but this was not statistically significant.

Respiratory infections may harm fetal development

Why was there a link between respiratory infections early in pregnancy and cardiac defects? According to the researchers, there are many potential reasons.

"For example, some infectious diseases may pass directly to the baby across the placenta, leading to problems in development," Dr. Chughtai said.

"Another reason is use of medications," Dr. Chughtai said. "The mother may need to take antibiotics or some other drugs to treat infections. These may indirectly affect the baby."

The researchers were not able to analyze the impact of medications taken by the mother to treat respiratory infection in this study. In future research, they plan to use Medicare and Pharmaceutical Benefits Scheme (PBS) data to do this.

"Moreover, if the mother has a fever due to infection, there are metabolic changes in the body, and these metabolites may cross the placenta which may affect the baby," Dr. Chughtai said. "High fever may also impair protein synthesis and causes cell death, resulting in congenital anomalies."

Impacts of COVID-19

Several other questions remain, including the impacts of COVID-19, which emerged after the study period of 2001–2016.

"Of course, it's an interesting question and we want to address this issue in a follow-up study," Dr. Chughtai said.

"So far from other studies there is no evidence that COVID-19 increases the risk of congenital abnormalities. But this is only initial research."

Implications for pregnancy

The researchers recommend avoiding respiratory infections during pregnancy as much as possible, to protect against congenital abnormalities.

"There are well-established risk factors, for example, X-rays and smoking, but infection is also a risk," Dr. Chughtai said.

"One of the important methods of prevention is influenza vaccination, which is available and effective and very safe in pregnant women."

More information: Abrar A. Chughtai et al, Associations between severe and notifiable respiratory infections during the first trimester of pregnancy and congenital anomalies at birth: a register-based cohort study, *BMC Pregnancy and Childbirth* (2023). DOI: 10.1186/s12884-023-05514-8

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