NEWS

Autism’s link to flu during pregnancy may be a fluke

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Women who come down with influenza while pregnant are no more likely than those without the infection to have a child with autism, according to a study of nearly 200,000 mother-child pairs[1].

The findings contradict studies that suggested **influenza infections during pregnancy** double the chances of having a child with autism. They also indicate that receiving a flu shot during pregnancy has no effect on autism risk. The U.S. Centers for Disease Control and Prevention recommends that pregnant women be **vaccinated against the flu**.

“Our findings should be reassuring to pregnant women,” says lead investigator **Lisa Croen**, director of the Autism Research Program at Kaiser Permanente in Oakland, California.

The new study does not challenge evidence that infections of other types increase autism risk. Pregnant women who have severe infections show a small increase in their **odds of having a child with autism**. (Some data suggest that the mother’s **immune response to the infection** affects her baby’s brain.)

The link to maternal influenza is much less robust. A 2012 study of nearly 100,000 mother-child pairs in Denmark found that women who **recalled having had the flu while pregnant** were nearly twice as likely to have a child with autism as women who did not have the flu. But three smaller studies published since then did not find a connection.

The 2012 study relied on self-reports, which can be unreliable, says **Judy Van de Water**, professor of internal medicine at the University of California, Davis, who was not involved in the work. “Sometimes people think they have influenza, but they don’t; they just have flu-like symptoms.”

Record numbers:

Croen and her colleagues instead analyzed medical records of children born in the Kaiser Permanente healthcare system in Northern California between 2000 and 2010. They focused on the 196,929 children who remained in the system until they were at least 2. This is the earliest age at which autism can reliably be diagnosed.

About 1,400 of the children were born to women diagnosed with the flu while pregnant, and more than 45,000 to women who received a flu shot while pregnant. About 3,100 of the children have a diagnosis of autism.

The researchers controlled for other autism risk factors, such as **premature birth**, **gestational diabetes** and **obesity** or **high blood pressure** in the mother. They found that children born to pregnant women with the flu were no more likely to have autism than those born to healthy women. The results were published 28 November in *JAMA Pediatrics*.

The researchers did see a 20 percent increase in risk for women who received a flu vaccine during the first trimester of pregnancy. But statistical tests suggest the findings arose by chance or as a result of some confounding factor that was unaccounted for, says investigator **Ousseny Zerbo**, a postdoctoral fellow at Kaiser.

Fluky findings:

The new study is unlikely to be the last word on the subject. Using medical records to identify trends is more reliable than asking women to remember details of their pregnancy. But the approach can miss women with mild infections or those who got their flu shots somewhere other than at their doctor's office, Zerbo says.

It is also possible that pregnant women who were **hospitalized with the flu** are the ones at risk of having a child with autism.

"Not all infections are equal," says **Brian Lee**, associate professor of epidemiology and biostatistics at Drexel University in Philadelphia. Lee led a 2014 study on severe infections during pregnancy, but was not involved in the new work. "Maybe it's some specific aspect of infection, such as severity, type of immune response or genetics, that tips the balance of risk."

Another aspect of infection that warrants investigation is **fever**, Zerbo says. A fever accompanying the flu may signal an **immune response that is severe enough** to raise the risk of autism.

REFERENCES:

1. Zerbo O. *et al. JAMA Pediatr.* Epub ahead of print (2016) **PubMed**