Study finds association between antidepressant use in pregnancy and diagnosis of psychiatric disorder

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Antidepressant use during pregnancy is associated with increased risk of psychiatric disorder diagnosis in children compared to children born to

mothers with no record of antidepressant use during pregnancy, finds a study published in *The BMJ* today.

However, the researchers stress that this finding should be interpreted with caution as the association may be due to the mother's underlying illness combined with antidepressant exposure in the womb.

Depression is common in women of childbearing age, and antidepressants have been increasingly used during pregnancy in the past few decades, with approximately 2-8% of pregnant women receiving this treatment.

Several studies have investigated whether the use of one type of antidepressant medication (selective serotonin reuptake inhibitor or SSRIs) during pregnancy is associated with autism spectrum disorder in offspring, although results have been conflicting.

Researchers have previously thought that SSRIs cross the placental barrier and affect the development of a baby's brain. If this holds true, exposure to SSRIs and other classes of antidepressants in the womb (in utero) may increase risk for a wider range of psychiatric disorders besides autism spectrum disorder.

So an international research team, led by Xiaoqin Liu at Aarhus University in Denmark, set out to investigate the association between in utero exposure to antidepressants and risk of psychiatric disorders.

The researchers analysed data from 905,383 children born between 1998 and 2012 in Denmark and followed up for a maximum of 16.5 years.

Children were categorised into four groups according to mothers' antidepressant use within two years before and during pregnancy: unexposed, antidepressant discontinuation (use before but not during

pregnancy), antidepressant continuation (use both before and during pregnancy), and new user (use only during pregnancy).

Overall, psychiatric disorders were diagnosed in 32,400 children. The authors found that the 15 year risk of a psychiatric diagnosis in children was 8% when their mothers had not been exposed to antidepressants at all.

After adjusting for several potentially influencing factors, the researchers found a small increased risk for psychiatric disorders among children of mothers who used antidepressants before and/or during pregnancy (11.5% and 13.6%). They also observed an increased risk of psychiatric disorders in children whose mothers continued antidepressant use during pregnancy (14.5%).

Results remained largely unchanged after further sensitivity analyses.

These associations "could be attributable to the severity of the underlying maternal disorders in combination with in utero antidepressant exposure, because mothers with severe symptoms are more likely to continue treatment during pregnancy," explain the authors.

This is an observational study, so no firm conclusions can be drawn about cause and effect, and the authors outline some study limitations which could have introduced bias. However, strengths include the large sample size and the long follow-up period.

The researchers acknowledge that the decision to discontinue or maintain antidepressant treatment during pregnancy is challenging, and say any final decision on antidepressant continuation "should be individualised and made jointly by health professionals and patients."

The researchers add that "focusing solely on a single psychiatric disorder among offspring in studies of in utero antidepressant exposure may be too restrictive."

In a linked editorial, Professor Hedvig Nordeng and colleagues from the University of Oslo emphasise that long term neurodevelopmental outcomes are needed to understand the safety of drugs taken during pregnancy.

It is important, they say, that researchers report absolute risks to facilitate communication between clinicians and pregnant women, as Liu and colleagues have done in their paper. "For example, if prenatal exposure to antidepressants is associated with a 23% increased risk of autism in children, and assuming a baseline prevalence of autism of 1%, then for every 10,000 women who continue treatment during pregnancy 23 additional cases of autism would occur. This number may be alarming to some patients and reassuring to others."

"Observational studies, for all their flaws, are a necessary piece of the puzzle, and healthcare databases such as the one used for this study provide a rich resource, particularly if they are augmented by additional data sources to reduce confounding," the authors write.

But these studies still need to be supplemented with data from a range of other types of research, including laboratory, animal, and genetic studies, to obtain a more complete picture of the mechanisms by which drugs may act on the developing fetus, the authors conclude.

More information: Antidepressant use during pregnancy and psychiatric disorders in offspring: Danish nationwide register based cohort study, www.bmj.com/content/358/bmj.j3668

Editorial: Prenatal exposure to antidepressants and increased risk of

psychiatric disorders, www.bmj.com/content/358/bmj.j3950