

Inducing and augmenting labor may be associated with increased risk of autism

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Pregnant women whose labors are induced or augmented may have an increased risk of bearing children with autism, especially if the baby is male, according to a large, retrospective analysis by researchers at Duke Medicine and the University of Michigan.

The findings, published in *JAMA Pediatrics* on Aug. 12, 2013, do not prove cause and effect, but suggest the need for more research, particularly as <u>labor</u> induction and augmentation have been used more frequently in recent years.

Expediting <u>deliveries</u> has benefitted women with <u>health conditions</u> that pose a risk to them and their unborn children. Inducing labor (stimulating contractions before the onset of spontaneous labor) and augmenting labor (increasing the strength, duration or frequency of contractions during labor) have been shown to prevent complications, including stillbirth.

"Inducing or augmenting labor has been previously suggested as a contributing factor to autism development," said lead author Simon G. Gregory, PhD, associate professor of medicine and medical genetics at Duke. "However, these studies produced conflicting results and consisted of a relatively small number of subjects. Our study is by far the largest one of its kind to look at the association between autism and induction or augmentation."

In this study, the researchers looked at records of all births in North



Carolina over an eight-year period and matched 625,042 births with corresponding public school records, which indicated whether children were diagnosed with autism.

Approximately 1.3 percent of male children and 0.4 percent of female children had autism diagnoses. In both male and female children, the percentage of mothers who had induced or augmented labor was higher among children with autism compared with those who did not have autism.

The findings suggest that among male children, labor that was both induced and augmented was associated with a 35 percent higher risk of autism, compared with labor that received neither treatment. This estimated increase in risk accounted for established maternal and pregnancy-related risk factors, such as maternal age and pregnancy complications. While induced labor alone and augmented labor alone were each associated with increased risk among male children, only augmentation was associated with increased risk among female children. The reason for the difference in findings between male and female children requires further investigation.

Gregory said the increased risk associated with induction and augmentation is similar to other known risk factors for developing autism, including a mother being older or a baby being born before 34 weeks of age. Additional analysis suggests that the absence of induction and augmentation might eliminate two in every 1,000 autism cases among male children born to induced or augmented mothers.

Autism – a developmental disability that can cause social, communication and behavioral challenges – affects approximately one in 88 children in the United States. Researchers and families alike are interested in understanding whether environmental factors may contribute to developing autism, particularly those that might affect the



developing brain.

"The scientific community has long looked for environmental contributors to the rising rates of autism in the United States," said Marie Lynn Miranda, PhD, senior author and dean of the University of Michigan School of Natural Resources and Environment. "This study provides preliminary evidence of an association between autism and labor induction/augmentation, especially among male children."

At the same time, Miranda cautioned that further investigation is warranted to understand these preliminary results. "Additional studies are needed to differentiate among potential explanations of the association, such as: underlying pregnancy conditions requiring the eventual need to induce/augment, the events of labor and delivery associated with induction/augmentation, and the specific treatments and dosing used to induce/augment labor (e.g., exogenous oxytocin and prostaglandins)," Miranda said.

In this study, researchers noted that children later diagnosed with autism were also more likely to undergo a <u>birth</u> characterized by fetal distress.

"The findings of this study must be balanced with the fact that there are clear benefits associated with induction and augmentation of labor," said study author Chad A. Grotegut, M.D., assistant professor of obstetrics/gynecology at Duke Medicine. "Labor induction, especially for women with post-date pregnancies or medical conditions such as diabetes and high blood pressure, has remarkably decreased the chance of stillbirth."

The authors stress that these findings do not support any deviation from the current standard of care for using induction and/or augmentation until further research is performed.



"Over the last decade or so, it has become clear that a combination of genetic and environmental risk factors contribute to risk for autism," said Alycia Halladay, PhD, senior director of environmental and clinical sciences at Autism Speaks, who was not involved in the study. "It is important for research to identify these <u>risk factors</u> so that the impact of these factors can be prevented."

"This is a provocative finding that calls for more research on the use of induction and augmentation during labor as a potential risk factor for autism," Halladay said. "The next step will be to understand why there is this association. Are there other factors at play here that led to the need for induction, for example? More research is needed before these results can be used to inform clinical practice."

The researchers noted that some information that could have benefitted their analyses was not available, including detailed data on the children's autism diagnoses. No information was available on the severity of autism, nor were records available for <u>children</u> diagnosed with <u>autism</u> who did not attend a public school. The researchers also did not have access to the full maternal or child medical records, which would provide more detailed information on the pregnancy and events of labor and delivery.

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