Researchers quantify the damage of alcohol by timing and exposure during pregnancy

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Prenatal exposure to alcohol is associated with a spectrum of abnormalities, referred to as Fetal Alcohol Spectrum Disorders. Physical features of the more serious Fetal Alcohol Syndrome (FAS) include smooth philtrum, thin vermillion border, short palpebral fissures, microcephaly, and growth deficiencies in weight and height. A new study has specified how specific quantities of alcohol exposure, patterns of drinking, and timing of exposure can have an impact on each of these features.

Results will be published in the April 2012 issue of *Alcoholism: Clinical & Experimental Research* and are currently available at Early View.

"This study was designed to address two challenges in FAS studies," said Haruna Sawada Feldman, a post-doctoral student in the department of pediatrics under the mentorship of professor Christina Chambers at the University of California, San Diego. "The first challenge concerned obtaining accurate alcohol exposure history from maternal reports that might involve social stigma and recall bias. This study collected information during pregnancy when women were unaware of their pregnancy outcome. The data were also collected by trained counseling specialists who had built a rapport with the woman and guaranteed confidentiality while collecting sensitive information. Finally, data were collected with specific details about timing in gestation, dose and pattern."

The second challenge concerned the quality of information on specific

physical features of FAS. "These alcohol-related features are often subtle, and a non-expert examiner may miss or misclassify features, and/or can be biased by subjectivity, especially if he/she suspects or knows about prenatal alcohol exposure (PAE)," said Feldman. "This study used an exposure-blinded expert dysmorphologist to look for these features. Furthermore, potential bias due to subjectivity was reduced because these examinations were conducted in the context of a larger study of more than 70 agents of interest, only one of which was alcohol."

"Research that links the quantity, frequency and timing of alcohol consumption during pregnancy among humans is virtually non-existent," added Philip A. May, a research professor in the Gillings School of Global Public Health at The University of North Carolina. "While animal data exist, studies like this one in humans are greatly needed, because extrapolation of concepts from animal models to humans is fraught with complications and problems of translation."

Feldman and her colleagues used data gathered on 992 women and their singleton infants in California between 1978 and 2005, examining patterns of drinking and timing of alcohol exposure in relation to selected FAS features. Structural features were assessed by a dysmorphologist who performed a blinded physical examination of all infants. Patterns of drinking were evaluated by drinks per day, number of binge episodes, and maximum number of drinks. Timing of exposure was evaluated zero to six weeks post-conception, six to 12 weeks post-conception, and during the first, second, and third trimesters.

"Higher PAE in every pattern we examined was significantly associated with an increased risk for having an infant born with reduced birth length or weight or having a smooth philtrum or thin vermillion border or microcephaly," said Feldman. "The most significant associations were seen during the second half of the first trimester; for every one drink increase in the average number of drinks consumed daily, there was a 25

percent increased risk for smooth philtrum, a 22 percent increased risk for thin vermillion border, a 12 percent increased risk for microcephaly, a 16 percent increased risk for reduced birth weight, and an 18 percent increased risk for reduced birth length."

"This paper clearly illustrates that drinking alcohol, especially binge drinking, during the first seven to 12 weeks of gestation is associated with four of the most important facial features characteristic of FAS as well as reductions in birth length and weight that are also characteristic of infants and children with FAS," said May. "This study also illustrates clearly that there is no threshold that triggers these features of FAS. Instead there is variability from woman to woman in the level of drinking that produces these features."

Feldman added that the lack of associations found during first-half of the first trimester between alcohol and outcomes should not be interpreted to mean that alcohol consumption during this time period is somehow safe. "Due to the study design, we were only able to include women who gave birth to live infants," she said. "Therefore, we did not include women who may have had miscarriages or stillbirths. It is important to know that alcohol-exposed infants who would have exhibited alcohol-related minor malformations might also be more likely to be lost to miscarriage following exposure during the first six-week window."

Both Feldman and May believe these findings reinforce the warning that there is no "safe" level of alcohol consumption during pregnancy. "Clinicians should continue to follow the recommendations to encourage women who are planning a pregnancy or have the potential to become pregnant to avoid alcohol, and to advise women who become pregnant to stop alcohol consumption," said Sawada. "These new findings can also help clinicians quantify the importance of discontinuing alcohol as early as possible."