Overall risk of birth defects appears low for women taking antiretrovirals during early pregnancy

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Among pregnant women infected with HIV, the use of antiretroviral (ARV) medications early in pregnancy to treat their HIV or to prevent mother-to-child transmission of HIV does not appear to increase the risk of birth defects in their infants, according to a new study led by Harvard School of Public Health (HSPH). It is one of the largest studies to date to look at the safety of ARV use during pregnancy.

While the study found that overall risk was low—in keeping with previous research that has found ARV use in pregnancy to be generally safe—the researchers did find that one ARV drug, atazanavir, was associated with increased risk of birth defects and they said it should be studied further.

"This study suggests that the benefits of using ARVs during pregnancy still far outweigh the risks for HIV-infected women, although they also indicate a need for continued monitoring," said Paige Williams, senior lecturer on biostatistics at HSPH and the study's lead author.

The study will appear online November 10, 2014 in *JAMA Pediatrics*.

While the use of combination ARV regimens among HIV-infected pregnant women has helped substantially reduce the number of HIV-infected infants, there remain concerns about the safety of in utero exposures to these medications—particularly as newer drugs are

approved and as an increasing percentage of women become pregnant while already taking ARVs.

The researchers looked at first-trimester exposures to ARVs in a group of 2,580 HIV-exposed, uninfected children enrolled between 2007 and 2012 in an ongoing U.S. study that follows HIV-infected pregnant women and their children—the Pediatric HIV/AIDS Cohort Study (PHACS) Surveillance Monitoring of ART Toxicities (SMARTT) study.

Few individual ARVs and no classes of drugs were associated with increased risk of birth defects, the researchers found. However, when atazanavir was used by mothers during pregnancy, risk of birth defects appeared to increase by about two-fold, particularly musculoskeletal and skin anomalies. Since most women receive a combination of three or more ARV drugs during pregnancy, the researchers also looked at what other drugs were commonly used together with atazanavir. When atazanavir was used with newer drugs, such as tenofovir or emtricitabine, the risk of birth defects remained higher, but there was no significant elevation in risk when atazanavir was used with older ARV drugs like zidovudine or lamivudine.

"As World Health Organization 2013 ARV guidelines are implemented globally, an increasing percentage of women with HIV will be expected to enter pregnancy already receiving ARVs. This heightens the need to identify optimal regimens based on their safety profiles as well as their effectiveness in preventing HIV transmission," said Williams.

More information: "Congenital Anomalies and In Utero Antiretroviral Exposure in Human Immunodeficiency Virus-Exposed Uninfected Infants, Paige L. Williams, Marilyn J. Crain, Cenk Yildirim, Rohan Hazra, Russell B. Van Dyke, Kenneth Rich, Jennifer S. Read, Emma Stuard, Mobeen Rathore, Hermann A. Mendez, and D. Heather Watts, for the Pediatric HIV/AIDS Cohort Study, *JAMA Pediatrics*,

online Nov. 10, 2014, DOI: 10.1001/jamapediatrics.2014.1889