First trimester growth: is it influenced by cigarette smoking, and other substances?

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Embryonic development is a complex process and chemical injury can lead to developmental problems. Exposure to some substances during pregnancy such as tobacco or cannabis is associated with significant adverse outcomes.[1,2,3,4] There are other commonly used substances that may have some positive or negative effects on early pregnancy growth and these include caffeine[5] and curcumin in curry.[6] Some studies have shown that early pregnancy development may have significant effects on pregnancy outcome[7,8] and also lifelong consequences.[1] Interventions such as behavioural modification can prevent the negative effects[9] of, for example, tobacco-smoking and cannabis.

In many countries the rate of smoking has recently decreased,[10] perhaps due to increased knowledge of its harmful effects, nevertheless, 22% of reproductive-age women still continue to smoke in the USA.[11] Knowledge of these hazards and public awareness can reduce the complications and improve public health. Cigarette smoking in pregnancy is associated with the risk of placental abruption, placenta praevia, low birth weight and preterm birth which can lead to significant morbidity and mortality in babies and have lifelong consequences.[1] Tobacco smoke affects the placenta,[12] through vasoconstriction and hypoxia[13] and at the level of DNA and mitosis of cells.[13,14] Is it possible to detect subtle changes using transvaginal ultrasound in the growth pattern of the developing embryo on first trimester ultrasound?

The existence of a relationship between first trimester growth and the risk of small for gestational age (SGA) infants has been known for many years. In 1998, Smith, *et al.*[15] published a large series of over 4200 pregnancies where the embryo was 2–6 days behind in expected crown rump length (CRL) and showed an increased relative risk for SGA birth. Likewise, in 2011 Salomon, *et al.*[16] studied 317 in-vitro fertilisation pregnancies where the gestational age could be accurately calculated and showed that CRL z-score correlated with birth weight.

Alcohol is a teratogen that causes a range of effects depending on the exposure timing and the amount of alcohol consumed. It readily crosses the placenta, and fetal blood alcohol levels rise to levels proportionate to maternal levels within one hour. No safe level of alcohol intake has been determined. One of the best-described and most severe outcomes of heavy maternal drinking is the fetal alcohol syndrome, characterised by a specific pattern of craniofacial malformations, prenatal and postnatal growth retardation, and central nervous system disorders. Studies have also indicated that alcohol consumption during pregnancy increases the risk of spontaneous abortion, reduced birth weight, intrauterine growth restriction, premature birth, cerebral palsy and infant oral cleft. The adverse behavioural effects of alcohol exposure during the second and third trimester are well documented; less clear is whether early first trimester-equivalent exposures also alter behaviour.

Despite increasing public health concerns, cannabis remains the most commonly used illicit drug among women of childbearing in developed countries, including the United States and Australia.[17,18] In 2007 a national survey, 30% of Australian females aged 14 years or older have used cannabis at some time in their lives. Of the same Australian women, 6.6% reported they had used cannabis in the past 12 months with a higher proportion reported by women of childbearing ages.[3,19] The main cannabis ingredient, tetrahydrocannabinol, can cross the placenta and directly affects the fetus.[4,20,21] Persistent use of cannabis may cause decreased uteroplacental perfusion,[4,20,21,22] intrauterine fetal growth restriction, deficit in birth weight and body length, as well as more likely admission to neonatal intensive care unit.[4,20,21,22] It has also been reported that cannabis may increase the risk of anencephaly.[23]

Caffeine is a widely used and accepted to be a pharmacologically active substance. The prevalence of exposure is > 80% in most western countries.[24] Caffeine freely passes the placenta and accumulates in the fetus.[25,26] The principal caffeine metabolism enzyme, cytochrome CYP1A2, is absent in placenta and fetus.[27] Also caffeine metabolism in pregnant women is three times slower than in non-pregnant women.[28] Fetal exposure to caffeine increases circulating catecholamine concentrations, which might subsequently lead to fetoplacental vasoconstriction and hypoxia and eventually affect fetal growth and development.[29,30] Studies have shown that heavy caffeine intake during pregnancy is associated with increased risk of miscarriage, fetal death and a lower birth weight.[31,32,33] One study showed that mothers who consumed > six caffeine units/day had a smaller first trimester CRL and a smaller third trimester femur length.[31]

With the use of sensitive high resolution ultrasound technology, the goalposts are shifting earlier and earlier when it comes to the detection of fetal abnormalities. These advances are also contributing to the potential for earlier detection of changes to early embryonic growth. In time, the potential negative influences of the aforementioned substances on first trimester growth may also become part of the routine early pregnancy ultrasound assessment.

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