and protein expression for the novel combination of KCNQ3 and KCNE5 are increased in term and preterm pre-eclampsia (PE) compared to normotensive control placentae [1]. The expression of these isoforms in early placental tissue has not been examined.

Objectives: The aims of this study were to determine whether KCNQ3 and KCNE5 mRNA and proteins are expressed in first trimester placental tissue.

Methods: Placental samples were obtained from women undergoing elective surgical termination of pregnancy between 6 and 12 weeks' gestation (n = 7) following informed written consent. KCNQ3 and KCNE5 mRNA expression was measured by qRT-PCR and normalised to stably expressed GAPDH. Immunohistochemistry was used to assess protein expression and localisation of the isoforms.

Results: Both mRNA and protein expression of KCNQ3 and KCNE5 were detected in placental tissue at all gestations. KCNE5 mRNA expression remained constant between 6 and 10 weeks with a subsequent rise at 11 and 12 weeks. KCNQ3 mRNA expression was initially lower than KCNE5 but markedly increased at 7 weeks remaining high until 10 weeks and falling below KCNE5 levels by 12 weeks. Protein expression for both KCNQ3 and KCNE5 was localised mainly to the syncytiotrophoblast but was also evident in the mesenchyme; overall KCNQ3 intensity significantly increased with gestational age (p = 0.044).

Conclusion: KCNQ3 and KCNE5 channel isoforms are highly expressed in first trimester placentas. The temporal changes in mRNA expression mirror changes in the placental tissue oxygen tension which increases between 8 and 10 weeks. This would precede the dislocation of the spiral artery plugs enabling maternal blood to flow freely and continuously into the intervillous spaces. We speculate that the increase in mesenchymal protein expression may be related to angiogenesis during this critical window of feto-placental vascular development. Future work will characterise the complete KCNQ/KCNE isoforms in first trimester placental tissue and assess potential functional roles of these channels both in early placentation and in relation to PE.

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Disclosure of interest

None declared.

References


OS082. CHIPS-Child: Testing the developmental origins hypothesis

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Introduction: CHIPS-Child is a natural test of the Developmental Origins of Health and Disease hypothesis (DOHaD) [1,2]. Reduced fetal growth rate is associated with adult cardiovascular risk markers (e.g., obesity) and disease [3,4]. Evidence worldwide indicates that this relationship is independent of birth weight. The leading theory describes ‘developmental programming’ in utero leading to permanent alteration of the fetal genome. While those changes are adaptive in utero, they may be maladaptive postnatally.

Objectives: To directly test, for the first time in humans, whether differential blood pressure (BP) control in pregnancy has developmental programming effects, independent of birth weight. We predict that, like famine or protein malnutrition, ‘tight’ (vs. ‘less tight’) control of maternal BP will be associated with fetal under-nutrition and effects will be consistent with developmental programming.

Methods: CHIPS-Child is a parallel, ancillary study to the CHIPS randomized controlled trial (RCT). CHIPS is designed to determine whether ‘less tight’ control [target diastolic BP (dBP) 100 mm Hg] or ‘tight’ control [target dBP 85 mm Hg] of non-proteinuric hypertension in pregnancy is better for the baby without increasing maternal risk.

CHIPS-Child will examine offspring of CHIPS participants non-invasively at 12 m corrected post-gestational age (±2 m) for anthropometry, hair cortisol, buccal swabs for epigenetic testing and a maternal questionnaire about infant feeding practices and background. Annual contact will be maintained in years 2–5 and will include annual parental measurement of the child’s height, weight and waist circumference.

CHIPS will recruit 1028 women. We estimate that 80% of CHIPS centres will participate in CHIPS-Child, approximately 97% of babies will survive, and 90% of children will be followed to 12 m resulting in a sample size of 626. Power will be >80% to detect a between-group difference of ≥0.25 in ‘change in z-score for weight’ between birth and 12 m (2-sided alpha = 0.05, SD 1).

Results: Recruitment has begun. The primary outcome will be the between-group difference in early postnatal weight gain (‘change in z score for weight’) between birth and 12 m (p < 0.05). Secondary: outcomes are (i) hypothalamic pituitary adrenal axis function (hair cortisol for overall cortisol production); and (ii) between-groups differences in DNA methylation, using targeted (genes associated with growth, obesity, cardiovascular disease, and/or a developmental programming effect) and global (genome-wide microarray) methods.

Conclusion: CHIPS-Child offers a unique opportunity to both clarify whether differential dBP control in pregnancy has developmental programming effects and contribute to our understanding of human biology and diversity in a way that a cross-sectional or other observational studies cannot.

Disclosure of interest

None declared.
References


OS083. Fetal growth and maternal vascular function in early pregnancy
C. Iacobaeus, G. Jörneskog, T. Kahan, M. Thorsell, E. Andolf (Department of Clinical Sciences, Karolinska Institutet, Danderyds Hospital, Danderyd, Sweden)

Introduction: Increasing evidence indicates that the rate of fetal growth is partly determined already in the first half of pregnancy. A number of authors have reported that if the fetus is smaller than expected at dating, the risk for a small for gestational age fetus increases.

Objectives: To investigate if maternal vascular function in early pregnancy reflects fetal growth in the first trimester.

Methods: Fifty healthy women with singleton viable pregnancies were included in the study that were recorded the ultrasound department of UltraGyn Stockholm, Sweden for ultrasound dating in gestational week 11–14. Of these, 25 pregnancies were included in the study that were recorded the early pregnancy reflects fetal growth in the first trimester.

Results: Fetuses that were smaller than expected at ultrasound dating compared to last menstrual period at gestational week 11–14, had an increased change in maximum sound dating compared to last menstrual period at gestational week 11–14. Of these, 25 ultrasound department of UltraGyn Stockholm, Sweden for

Disclosure of interest
None declared.


OS084. Maternal haemodynamics at 11–13 weeks of gestation and adverse pregnancy outcomes
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Introduction: Women who develop adverse pregnancy outcomes are at increased risk of cardiovascular disease. In individuals with cardiovascular disorders there is increased central aortic systolic blood pressure (SBP Ao) and arterial stiffness.

Objectives: The hypothesis is that increased SBP Ao and arterial stiffness are apparent before the clinical onset of adverse pregnancy outcomes.

Methods: This was a prospective study in singleton pregnancies at 11th–13th weeks’ gestation. Pulse wave velocity (PWV), augmentation index (Alx) and SBPAo were measured. At the same visit, we recorded maternal characteristics and medical history and performed combined screening for aneuploidies. We also measured the uterine artery Doppler pulsatility index (PI). The study outcomes included preeclampsia (PE), gestational hypertension (GH), gestational diabetes (GDM), small for gestational age (SGA) and preterm delivery (PTD). The diagnosis of PE and GH was made according to the guidelines of the International Society for the Study of Hypertension in Pregnancy. The neonate was considered SGA if the birth weight was less than the 5th percentile for gestation at delivery. The diagnosis of GDM was made if the fasting plasma glucose level was at least 6 mmol/L or the plasma glucose level 2 h after oral administration of 75 g glucose was 7.8 mmol/L or more (WHO). We compared these parameters in those that developed PE (n = 181), GDM (n = 105), GH (n = 137), SGA (n = 337), PTD prior to 37 weeks’ gestation (n = 354) with

Conclusion: In the first trimester, changes in vascular function might reflect important adaptations that are required to facilitate normal fetal growth. This was highlighted by the findings of a positive correlation between fetal growth at 11–14 weeks gestation and changes in endothelial dependent microcirculation.

Vascular function of these women will be followed longitudinally during pregnancy and related to obstetric outcome. If changes in microcirculation in the first trimester correlates to an increased risk for complications such as hypertensive disorders during pregnancy or intrauterine growth restriction this gives new insights into the early phase of these complications.
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