



The duration of sexual relationship and its effects on adverse pregnancy outcomes



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ABSTRACT

This study aims to determine if a short duration of sexual relationship is more common among women who experience adverse pregnancy outcomes including gestational hypertension (GHT), preeclampsia, small for gestational age (SGA) pregnancies and spontaneous preterm birth (sPTB) with or without abnormal uterine artery Doppler compared to women who have uncomplicated pregnancies. 5591 nulliparous women from the Screening for Pregnancy Endpoints (SCOPE) study were included. The risk for pregnancy complications for women who had a duration of sexual relationship of ≤ 3 months, 4–6 months, 7–9 months, 10–12 months was compared with women who had a duration of sexual relationship of > 12 months. Uterine artery Doppler was performed at 20 ± 1 weeks' gestation. A short duration of sexual relationship (≤ 3 months) was more common among women with SGA in the presence of abnormal uterine artery Doppler [9.8% vs 3.0%, aOR (95% CI) 3.4 (1.6–7.08)] compared to women who had uncomplicated pregnancies. A short duration of sexual relationship (≤ 3 months) was also more common among women who had abnormal uterine artery Doppler compared to those with normal uterine artery Doppler [6.1% vs 3.1%, aOR (95% CI) = 2.1 (1.4–3.2)]. A short duration of sexual relationship was not associated with preeclampsia after adjusting for confounders. A short duration of sexual relationship is more common among women who deliver SGA infants with features of placental insufficiency as indicated by abnormal uterine artery Doppler.

1. Introduction

Prolonged exposure to paternal antigens in seminal fluid induces a state of maternal active immune tolerance to the fetus which facilitates successful placentation (Martinez-Varea et al., 2014). A maladaptive maternal immune response is proposed to result in impaired trophoblast invasion of spiral arteries, a characteristic feature of placental fetal growth restriction with or without the maternal preeclamptic syndrome (Redman et al., 1999; Huppertz, 2015). Repeated exposure to semen from the biological father of the baby over a prolonged time leads to development of maternal mucosal tolerance to these paternal antigens (Robertson et al., 2003, 2002).

Martin and Herrmann in 1977 first reported that repeated exposure to semen from the biological father of the baby is associated with a reduced risk of preeclampsia (Marti and Herrmann, 1977). This was subsequently confirmed by other epidemiological studies which demonstrated that the duration of sexual cohabitation before conception was inversely related to the incidence of preeclampsia (Robillard et al., 1994; Einarsson et al., 2003; Saftlas et al., 2014) but refuted by another (Ness et al., 2004). We previously investigated the association between the duration of sexual relationship and its effects on gestational hypertension (GHT), preeclampsia and small for gestational age (SGA) pregnancies in a subset of the SCOPE (Screening fOr Pregnancy Endpoints study) cohort and found that a short duration of sexual

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relationship was more common among women who developed preeclampsia as well as among those women in the subgroup with SGA and abnormal uterine artery Doppler (Kho et al., 2009). In this study, we aim to investigate the above association in the entire SCOPE cohort and also that between a short duration of sexual relationship and other adverse pregnancy outcomes potentially associated with abnormal placentation namely spontaneous preterm birth (sPTB). Abnormal uterine artery Doppler waveform is a surrogate marker of impaired utero-placental perfusion. Therefore, we also aimed to investigate the association between a short duration of sexual relationship and abnormal uterine artery Doppler at 20 ± 1 weeks' gestation.

2. Materials and methods

The participants of this study were women who were recruited to the SCOPE study between November 2004 and February 2011 in Adelaide, Australia, Auckland, New Zealand, Manchester, Leeds and London, United Kingdom and Cork, Ireland. The SCOPE study (www.scopestudy.net) is an international, multicentre, prospective cohort study with the aim of developing screening tests to predict preeclampsia, SGA infants and sPTB across different populations. Ethics approval was gained from local ethics committees of each participating centre (Australia REC 1712/5/2008, New Zealand AKX/02/00/364, Manchester, Leeds and London 06/MRE01/98, Cork ECM5 (10)05/02/08) and all women provided written informed consent.

A previous study by Kho and colleagues investigated the effects of a short duration of sexual relationship and preeclampsia and SGA pregnancies in the first 2507 women in the Adelaide and Auckland cohorts of the SCOPE study which included 2507 women. Here, we have included women from the entire SCOPE cohort of 5591. Recruitment of participants to the SCOPE study has previously been described in detail (Kho et al., 2009). In brief, participants were referred from hospital antenatal clinics, obstetricians, general practitioners, community midwives or self-referred. Nulliparous women with singleton pregnancies were recruited before 15 weeks' of gestation. Those considered at high risk of preeclampsia, SGA or preterm birth because of underlying medical conditions (including known pre-existing chronic hypertension on hypertensive medication or with a blood pressure $> 160/100$ mmHg at 15 weeks of gestation), gynaecological history, three or more miscarriages or terminations of pregnancy or couples who received medical or surgical interventions which could modify pregnancy outcome were not eligible. Participants were interviewed at 15 ± 1 and 20 ± 1 weeks' of gestation by SCOPE research midwives.

Recruited women were excluded from the present analyses if any of the following reasons applied: protocol violation, lost to follow up, multiple sexual partners and unsure of the identity of the biological father of the baby and miscarriage or termination (Fig. 1). At the 15 ± 1 weeks' interview, data collected included demographic information, medical history, previous obstetric history, family history of obstetric complications and medical disorders. Current pregnancy data included information on any complications during current pregnancy, diet, smoking, alcohol and the use of recreational drugs. Details about the pre-pregnancy sexual history with the biological father of the index pregnancy including conception following the first episode of sexual intercourse and months of sexual relationship were obtained. The duration of sexual relationship was classified as conceived after a relationship of ≤ 3 months, ≤ 6 months and ≤ 12 months. Maternal physical measurements obtained at 15 ± 1 weeks of gestation included height, weight and blood pressure.

Uterine artery Doppler ultrasound was performed at 20 ± 1 weeks' gestation. Resistance indices (RI) for both uterine arteries were reported and the mean RI was calculated as the average of the two. If only a left or right uterine artery RI result was available, this was used as the mean RI. An abnormal uterine artery Doppler was defined as a mean resistance index > 90 th percentile (Groom et al., 2009). All participants were followed prospectively and pregnancy outcome data and infant

measurements were recorded by research midwives usually within 72 h of birth.

Gestational hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg on two or more measurements 6 h apart after 20 weeks of gestation. *Preeclampsia* was defined as gestational hypertension or postpartum hypertension with proteinuria (24-h urinary protein 300 mg or spot urine protein : creatinine ratio ≥ 30 mg/mmol creatinine or urine dipstick protein $\geq + +$) or any multisystem complication of preeclampsia. Multisystem complications included any of acute renal insufficiency defined as a new increase in serum creatinine concentration ≥ 100 μ mol/L antepartum or > 130 μ mol/L postpartum; effects on liver, defined as raised aspartate transaminase or alanine transaminase concentration, or both, > 45 IU/L and/or severe right upper quadrant or epigastric pain or liver rupture; neurological effects included eclampsia, imminent eclampsia (severe headache with hyper-reflexia and persistent visual disturbance), or cerebral haemorrhage; and haematological effects included thrombocytopenia (platelets $< 100 \times 10^9$ /L), disseminated intravascular coagulation, or haemolysis (North et al., 2011). *Small for gestational age (SGA)* was defined as a birth weight below the 10th customised centile adjusted for maternal height, weight, parity and ethnicity, gestational age at delivery and infant sex (McCowan et al., 2004). *SGA with abnormal Doppler* was defined as birth of a SGA infant where the mother had a mean uterine artery RI > 90 th percentile at 20 ± 1 weeks' gestation. *Spontaneous preterm birth (sPTB)* was defined as spontaneous preterm labour or preterm premature rupture of membranes resulting in a preterm birth at < 37 weeks. *Uncomplicated pregnancy* was defined as a pregnancy with no antenatal medical or obstetric complications and resulting in the delivery of an appropriately grown, healthy baby at ≥ 37 weeks' of gestation.

Statistical analyses were performed using R version 3.3.1 (cran.r-project.org). The data for each pregnancy complication (preeclampsia, preeclampsia with abnormal Doppler, gestational hypertension, SGA, SGA with abnormal Doppler and sPTB) was compared to the uncomplicated pregnancy group. For categorical variables, Chi-square test was used to compare the groups and for continuous variables, student's *t*-test or its non-parametric alternative was used as appropriate. Logistic regression was used to estimate odds ratios for each of the measures of variables of interest. For each variable, adjusted odds ratios were calculated by adding the following variables to the logistic regression model: maternal age, ethnicity, primigravidity, BMI, mean arterial blood pressure, smoking status at 15 ± 1 weeks' gestation and use of barrier contraception. The independent variable was the duration of sexual relationship and the dependent variable was the pregnancy outcome. Complete data were available for all variables analysed. Results are reported as number and percent [n (%)] or mean \pm standard deviation (SD) as appropriate. $P < 0.05$ was considered statistically significant. A retrospective power calculation was performed and demonstrated that we had $> 90\%$ power to detect the observed increase in risk in SGA with abnormal Uterine artery Doppler and also in the comparison between normal and abnormal Uterine artery Doppler.

3. Results

Of the 5690 pregnant women recruited, 5591 were eligible for this study (Fig. 1). Amongst these 5591, 3334 (59.6%) had uncomplicated pregnancies, 470 (8.4%) had gestational hypertension, 277 (4.9%) had preeclampsia, 628 (11.2%) had SGA infants, 234 (4.2%) had sPTB, 904 (16.2%) had other medical or obstetric complications including 173 (3.1%) with gestational diabetes mellitus (GDM). Of the 2257 women who had complicated pregnancies, 241 (10.7%) had more than one complication during pregnancy (Fig. 1).

The characteristics of the participants according to pregnancy outcome are shown in Table 1. A short duration of sexual relationship (≤ 3 months and 4–6 months) was more common among women who

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