**Journal of Neonatal Surgery**
***ISSN(Online): 2226-0439***
***Vol. 14, Issue 32s (2025)***
*https://www.jneonatalsurg.com*

OPEN ACCESS

# Peri-implantation Sexual Abstinence and Early Placental Positioning: A Randomized Controlled Trial of Placental Location and Pregnancy Outcomes

**Abubakar Ibrahim[1], Martina Irwan Khoo[2], Engku Husna Engku Ismail[1], Nik Syamim Firdaus Nik Ahmad Zuky[1], Nik Hazlina Nik Hussain[1], Anani Aila Mat Zin[3], Liza Noordin[4], Sarimah Abdullah[5], Zaleha Abdullah Mahdy[6], Nik Ahmad Zuky Nik Lah[1]**

[1]Department of Obstetrics and Gynaecology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[2]Department of Chemical Pathology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[3]Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[4]Department of Physiology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[5]Biostatistics and Research Methodology Unit, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia

[6]Department of Obstetrics and Gynaecology, Hospital Canselor Tuanku Muhriz UKM. Jalan Yaacob Latif Kuala lumpur, Bandar Tun Razak, 56000 Cheras, Wilayah Persekutuan Kuala Lumpur

**Corresponding author –**

Assoc Prof Dr Nik Ahmad Zuky Nik Lah

Department of Obstetrics and Gynaecology, School of Medical Sciences, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan

Email ID : nikzuky@usm.my

Cite this paper as Abubakar Ibrahim, Martina Irwan Khoo, Engku Husna Engku Ismail, Nik Syamim Firdaus Nik Ahmad Zuky, Nik Hazlina Nik Hussain, Anani Aila Mat Zin, Liza Noordin, Sarimah Abdullah, Zaleha Abdullah Mahdy, Nik Ahmad Zuky Nik Lah (2025) Peri-implantation Sexual Abstinence and Early Placental Positioning: A Randomized Controlled Trial of Placental Location and Pregnancy Outcomes..Journal of Neonatal Surgery, 14, (32s) 9747-9757

## ABSTRACT

**Introduction:** The peri-implantation period is critical for blastocyst implantation and placental development. Sexual intercourse during this phase may disrupt implantation, increasing the risk of low-lying placenta and adverse pregnancy outcomes. Evidence on whether peri-implantation sexual abstinence can influence placental positioning and maternal–fetal health is lacking.

**Methods:** We conducted a single-centre randomized controlled trial (Hospital Universiti Sains Malaysia, January 2021–October 2023). Couples were randomized 1:1 to either peri-implantation sexual abstinence (refraining from intercourse for 14 days post-ovulation) or non-abstinence. Pelvic ultrasound at 5–6 and 11–12 weeks assessed implantation, and serial ultrasounds at 18–22, 28–32, and 36–38 weeks monitored placental location and fetal growth. Maternal and neonatal outcomes, including preeclampsia, fetal growth restriction (FGR), preterm birth, NICU admission, and congenital anomalies, were recorded.

**Results:** Of 94 couples screened, 61 were randomized; 33 achieved confirmed pregnancies and entered primary analysis (abstinence n=9; non-abstinence n=24). Low-lying placenta occurred in 0/9 (0.0%; 95% CI 0–33.6%) in the abstinence group and 5/24 (20.8%; 95% CI 7.1–42.2%) in the non-abstinence group (absolute risk difference –20.8 percentage points; Fisher's exact test p=0.29). No preeclampsia or placenta previa were observed. Secondary outcomes showed no significant differences, though event counts were small.

**Discussion :** Peri-implantation sexual abstinence was associated with a lower point estimate of early low-lying placenta, though not statistically significant in this pilot trial. Findings suggest a potential biological signal warranting larger trials with objective adherence measures to test causality and refine strategies for reducing abnormal placentation.

**Trial Registration (JEPeM Code for ethical clearance):** USM/JEPeM/21030234 This study was registered on 7th July 2021 and conducted in accordance with the Declaration of Helsinki, ICH-GCP Guidelines, CIOMS Ethical Guidelines, and WHO Standards for Health Research Ethics Review.

**Keywords**: *Peri-implantation, sexual abstinence, low-lying placenta, placenta previa, fetal growth restriction, randomized controlled trial*

## 1. INTRODUCTION

The peri-implantation period is a critical phase of pregnancy, marked by intricate molecular and physiological interactions that determine successful blastocyst implantation and placental development (1). Implantation typically occurs 6–10 days after ovulation (2), and the blastocyst remains mobile in the uterine cavity for several days before stable attachment, a period during which the uterine environment is especially vulnerable to perturbation (3,4). Sexual intercourse during the peri-implantation window may be a double-edged phenomenon. On one hand, intercourse facilitates sperm transport and fertilization (5); on the other hand, observational and prospective data suggest intercourse during the peri-implantation window is associated with lower fecundability**,** possibly because it increases the risk of failed implantation (i.e., loss after fertilization but before clinical recognition) (6). Peri-implantation sexual intercourse is biologically active beyond sperm delivery and therefore represents a plausible, modifiable influence on implantation (6). Empirical evidence shows that intercourse increases intra-vaginal and intra-uterine pressures and stimulates myometrial contractions, effects that are augmented by female orgasm (6–9). Such contractions at the time when a blastocyst is still mobile (the blastocyst remains free in the uterine cavity for ~3 days before firm attachment (10)) could mechanically displace a loosely apposed embryo (6), cause shallow or incomplete attachment, expel the conceptus a plausible path to repeated implantation failure (RIF) or implantation at lower part of the cervix close to the uterus (6,11). Furthermore, uterine relaxants such as atosiban improve implantation and pregnancy rates to 43% in ART by suppressing contractions, supporting a causal role for myometrial activity in implantation outcomes (12). Placental positioning is a key determinant of pregnancy outcomes (13–15). A low-lying placenta, particularly in early gestation, might be a precursor to placenta previa, a condition associated with life-threatening hemorrhage, preterm birth, and emergency cesarean delivery (16,17). Although risk factors such as prior cesarean sections and advanced maternal age are well-established (18,19), the role of peri-implantation behaviors, including sexual activity, remains underexplored.

Recent studies have explored the immunological and oxidative impact of seminal fluid on the uterine environment, demonstrating its potential to trigger inflammation-like responses in cervical and endometrial tissues. (20–25). While this may have evolutionary roles in immune tolerance and maternal adaptation, it may also interfere with the delicate uterine environment during implantation Furthermore, the downstream effects on placental development, fetal well-being, and long-term pregnancy outcomes remain inadequately explored.

To our knowledge, no randomized controlled trials have evaluated the impact of peri-implantation sexual abstinence on the incidence of low-lying placenta and maternal-fetal outcomes in early and late pregnancy. Given the theoretical risk of disturbed implantation and placental malpositioning, it is critical to evaluate whether brief sexual abstinence during the peri-implantation window offers protective benefits. We hypothesized that peri-implantation sexual abstinence reduces the risk of low-lying placenta and improves maternal–fetal outcomes. This study provides the first clinical (RCT) evidence linking peri-implantation sexual behavior with placental development, offering a potential behavioral intervention to mitigate high-risk pregnancies.

## 2. METHODS

This randomized controlled trial (RCT) employed a parallel-group design and was conducted at the Departments of Obstetrics & Gynaecology and Pathology, Hospital Universiti Sains Malaysia (HUSM). Although originally scheduled to run from November, 2020, to October, 2023, the study experienced considerable delays due to the COVID-19 pandemic. The pandemic significantly disrupted participant recruitment, as many individuals avoided hospital visits, leading to slower-than-anticipated enrollment. Furthermore, the study's longitudinal nature required continuous monitoring of each participant from the preconception phase through to delivery, extending the duration of individual participation to nearly one year. These challenges collectively necessitated a revision and extension of the study timeline.

Eligible participants were healthy women aged 20 to 40 years with regular menstrual cycles (28–30 days) and no history of medical or gynecological conditions, including polycystic ovarian syndrome (PCOS) or endometriosis. Participants were required to comply fully with the study protocols.

Exclusion criteria encompassed current or past tobacco or alcohol use, a body mass index (BMI) outside the 18.5–30 kg/m² range, and any history of cardiovascular disease, chronic hypertension, respiratory or renal conditions, diabetes mellitus, prior preeclampsia, lower segment cesarean section, dilatation and curettage, or myomectomy.

## 3. RECRUITMENT AND EXCLUSION

Between July 2021 and October 2023, couples were recruited via flyers, media advertisements, and direct invitations. Eligibility was screened by telephone, and vulnerable populations were excluded. Both partners provided written informed consent after being briefed on the intervention, procedures, risks, benefits, and right to withdraw at any time. Couples were

informed that if pregnancy was not achieved after two menstrual cycles, they could withdraw without penalty. The study protocol and consent were approved by the institutional ethics board.

Participants received a modest honorarium and reimbursement for transport. All study-related clinical care (ultrasound scans, antenatal monitoring, obstetric management) was provided free of charge. Reasons for withdrawal, including non-conception, were recorded in the trial masterfile and are shown in the CONSORT diagram (Figure 1). Participants withdrawing for non-pregnancy reasons were excluded from the primary pregnancy-level analysis but described in ancillary analyses.

Given the behavioral nature of the intervention, staff monitored for relationship stress or social harms, and participants were provided with counseling contacts.

## 4. RANDOMIZATION AND OUTCOMES

A total of 94 couples were randomized (non-abstinence n=55; abstinence n=39). Thirty-four achieved a confirmed pregnancy (non-abstinence n=25; abstinence n=9). One abstinence participant was lost to follow-up, leaving 33 pregnancies for analysis (non-abstinence n=24; abstinence n=9). Because this was a preconception trial, we anticipated that not all randomized couples would conceive within the study period. Population studies report per-cycle fecundability of ~20–25%, with cumulative pregnancy probabilities of ~60% by three cycles and ~80% by six cycles, meaning a substantial proportion of randomized participants in preconception trials do not contribute a pregnancy outcome (9,26,27). Accordingly, we prespecified a pregnancy-level modified intention-to-treat (mITT) analysis, and effect estimates are presented with exact Clopper–Pearson confidence intervals rather than relying solely on p-values. Participant flow is illustrated in the CONSORT diagram Figure 1 Consort flow chart

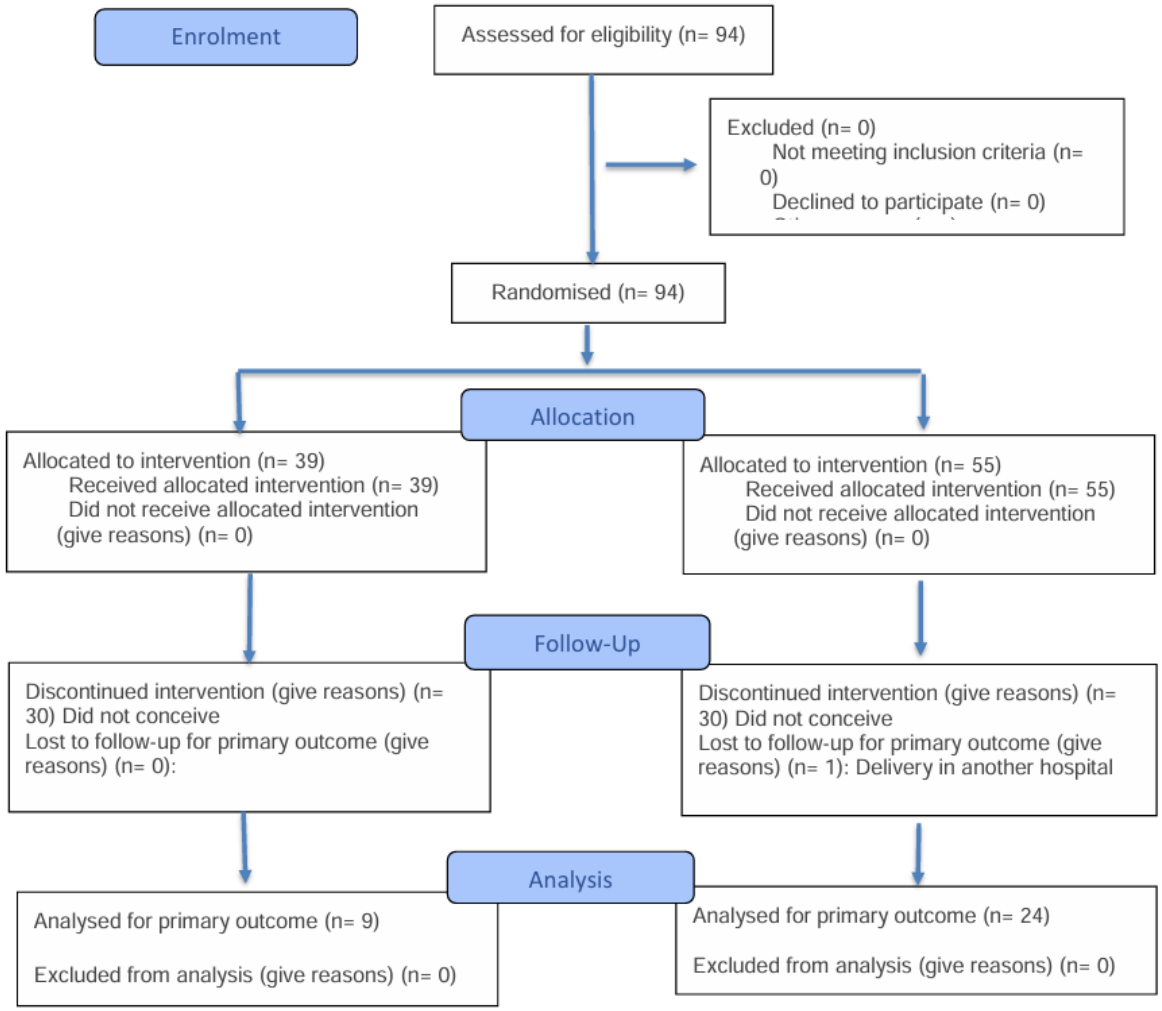


**Figure 1Consort flow chart**

**Sample size and power considerations**

The original sample-size calculation in the protocol used published preterm-birth rates associated with placenta previa to inform plausible effect sizes (Awad et al.). Using those data, the protocol estimated that approximately 30 pregnancies (≈22 control, 8 intervention) would be required to detect the large absolute effect hypothesised in the protocol (α=0.05, 80% power). Because pregnancy outcomes are only measurable among participants who conceive, the protocol therefore planned to recruit additional couples to allow for non-conception and other losses. In practice, although 94 couples were enrolled, natural pre-conception attrition reduced the pregnancy cohort to 34 (33 analysed). As a result, event counts for some outcomes (including preterm birth) are smaller than originally planned and confidence intervals are wide; inferential comparisons for rare events should therefore be interpreted with caution. We do not present post-hoc power; instead we report effect estimates with exact 95% confidence intervals so readers can judge precision directly.

**Randomisation, concealment and blinding**

A randomisation schedule was generated prior to participant enrolment using a computerised random number generator by an independent statistician not otherwise involved in participant recruitment or outcome assessment. Allocation codes were placed into sequentially numbered, opaque, sealed envelopes prepared and stored by the study research assistant. At the baseline visit the enrolling investigator (student researcher) opened the next sequential envelope in the presence of the participant and recorded the envelope number and date in the trial log. The person who prepared the randomisation envelopes did not perform outcome assessment or data analysis., Sonographers performing the ultrasound scans were blinded to treatment allocation. All ultrasound images used for the primary outcome were anonymised and assigned unique study identifiers before central review. Two independent senior sonographers (blinded to allocation and to each other's readings) centrally reviewed the stored transvaginal images to classify placental location. Any discordant classifications were resolved by consensus or adjudicated by a third blinded sonographer (Everything was done strictly following consort guidelines (28). Inter-rater agreement (Cohen's kappa) is reported in the Results. Outcome adjudication and final data analysis were performed by the student researcher and the PI; the statistician validated the key inferential analyses. All authors had full access to the final dataset and accept responsibility for the accuracy and completeness of the reported analyses.

**Protocol**

Ovulation was estimated to occur 14 days prior to the onset of the next menstrual cycle. Based on Wilcox et al. (2000) (9), the fertile window was defined as five days before to three days after the anticipated ovulation date. The peri-implantation window, according to Steiner et al. (2014) (6), spanned around 10 days post-ovulation. To predict ovulation, participants recorded the first day of their last menstrual period (LMP) and used daily ovulation predictor kits from cycle day 11 to 15, testing afternoon urine (between 12 PM and 6 PM) for the luteinising hormone (LH) surge. A positive LH test signaled ovulation within 24–36 hours. Timed intercourse with ejaculation inside the vagina was then carried out within 24 hours to enhance the chance of conception, in alignment with the fertility model proposed by Wilcox et al.., (9). This approach ensured consistent identification of the fertile period and accurate timing of conception across both study groups.

After this initial attempt, the non-abstinence group continued sexual activity as desired during the next 14 days, logging events in pregnancy booklets. The abstinence group refrained from further intercourse during this period.

**Adherence Monitoring:** Each participant was provided with a standardized monitoring booklet to document the first day of the last menstrual period (LMP), the day of ovulation (confirmed by a urinary LH surge test), and all instances of sexual intercourse. Prior to study commencement, both partners received thorough counseling on the peri-implantation abstinence protocol, LH testing procedures, and how to accurately complete the diary. During the peri-implantation phase, trained research staff maintained regular telephone contact with participants to reinforce adherence guidelines, ensure proper documentation, and confirm LH test outcomes. Participants assigned to the abstinence group were instructed to refrain from sexual intercourse for 14 consecutive days starting from the LH surge day, corresponding to the implantation window, while those in the non-abstinence group continued sexual activity without restriction. Booklet records were reviewed at each follow-up visit, and compliance was verified by cross-referencing diary entries with follow-up interviews. Complete adherence to the abstinence instructions was observed among all nine participants in the abstinence group.

Pregnancy was confirmed by missed menses and urine tests, followed by transvaginal ultrasound at 5–6 and 11–12 weeks to verify implantation. Subsequent transabdominal ultrasounds were performed at 18–22, 28–32, and 36–38 weeks to assess fetal growth, placental location, and anomalies. All scans were performed by trained sonographers. Deliveries occurred at Hospital USM with standardized obstetric care.

Pregnancy outcomes and complications were documented in pregnancy booklets. Couples not conceiving after two cycles could withdraw, per ethics approval, to minimize burden. The full protocol and amendments are provided in Supplementary File S1.

**Statistical Analysis**

The prespecified primary analysis population was the modified intention-to-treat (mITT) pregnancy cohort, defined as all randomized participants with a confirmed intrauterine pregnancy and first-trimester ultrasound. Results are presented as point estimates with exact 95% confidence intervals (Clopper–Pearson); no post-hoc power calculations were performed. All tests were two-sided at α=0.05.

Continuous variables were summarized as mean (SD) or median (IQR), with normality assessed by Shapiro–Wilk. Group comparisons used t-tests (Welch correction if unequal variances) or Mann–Whitney U tests. Categorical outcomes, including the primary endpoint (low-lying vs upper-segment placenta), were expressed as counts and percentages with Fisher's exact test. Absolute risk differences with 95% CIs (Newcombe method) and risk ratios were reported where informative.

Sensitivity analyses included: (1) strict ITT at the randomized-couple level, (2) per-protocol analysis of fully adherent participants, and (3) adjusted models controlling for maternal age, parity, and BMI. Penalized logistic regression (Firth correction) or exact logistic regression was applied where separation occurred.

Missing data for primary outcomes were analyzed by complete-case methods; details are shown in the CONSORT diagram. Secondary outcomes were considered exploratory and reported without multiplicity adjustment. Analyses were conducted in GraphPad Prism v8.4.3 and R v4.2.2

**Ethical Considerations**

This study adhered to the ethical principles outlined in the Declaration of Helsinki, the International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) standards, the Council for International Organizations of Medical Sciences (CIOMS) Guidelines, and the World Health Organization (WHO) Standards for Health Research Ethics Review. Ethical approval was granted by the Universiti Sains Malaysia (USM) Research Ethics Committee (JEPeM Code: USM/JEPeM/21030234). Written informed consent was obtained from all participants before enrollment, ensuring voluntary participation and the right to withdraw at any time. Confidentiality was ensured by anonymizing samples with unique codes; all available data were securely stored for up to three years. Adherence to the intervention was assessed through self-reported logs and structured antenatal interviews. Ultrasound monitoring was used to track fetal growth, placental position, and pregnancy progression. The official ethics approval letter is included in Supplementary File S2.

## 5. RESULTS

**Baseline Characteristics**

Baseline demographics are shown in

*Table 1* There were no statistically significant differences between arms by conventional testing (all $p > 0.05$). Because p-values are sensitive to sample size and can be misleading in small randomized samples, we additionally report standardized mean differences (SMDs) to describe baseline balance. SMDs indicated small–moderate imbalances for gravidity and parity (SMDs ≈ 0.42) and BMI (SMD ≈ 0.35). To account for these differences we present adjusted sensitivity analyses controlling for maternal age, parity and BMI; results were qualitatively similar to the unadjusted analyses

***Table 1*** **Baseline demographic and clinical characteristics of pregnancies included in the analysed cohort (mITT / per-protocol). Standardized mean differences (SMDs) and p-values are presented to describe between-group balance. Absolute SMD > 0.10 was considered potentially meaningful.**

| Characteristic | Abstinence (n = 9) | Non-abstinence (n = 24) | SMD (abstinence − non-abstinence) | p-value |
|---|---|---|---|---|
| Age, mean ± SD (range), years | 31.1 ± 4.2 (25–37) | 30.0 ± 5.3 (22–40) | 0.22 | 0.542 |
| Gravidity, mean ± SD (range) | 2.33 ± 0.87 (1–3) | 3.04 ± 1.89 (0–8) | −0.42 | 0.152 |
| Parity, mean ± SD (range) | 1.44 ± 0.73 (0–2) | 2.08 ± 1.72 (0–7) | −0.42 | 0.144 |
| BMI, mean ± SD (kg/m²) | 23.5 ± 1.6 | 24.2 ± 2.1 | −0.35 | 0.319 |

SMD = standardized mean difference. Negative SMD indicates the mean is higher in the non-abstinence group than in the abstinence group. Absolute SMD magnitudes: <0.10 negligible, 0.10–0.20 small, 0.20–0.50 moderate, >0.50 large. Continuous variables presented as mean ± SD (range). P-values are from independent t-tests; p-values are shown for completeness but SMDs are preferred for assessing baseline balance in small randomized trials.

**To determine the impact of peri-implantation sexual abstinence on the incidence of low-lying placenta in early pregnancy:** Placental location was categorised for analysis as either upper-segment or low-lying. Upper-segment placentas included posterior upper-segment, anterior upper-segment and fundal locations. Low-lying placenta was defined according to the prespecified protocol as placental edge ≤20 mm from the internal os on first-trimester ultrasound, a location associated with increased risk of placenta previa and related complications. Refer to Figure 2 A *bar-chart showing the distribution of placental positions:* Figure 3 A bar-chart showing the distribution of placental positions for a bar chart trends

of group and individual placental position.

**Results placental position:** Among the 33 pregnancies included in the prespecified pregnancy-level analysis, no cases of low-lying placenta were observed in the abstinence arm (0 of 9; 0.0%, Clopper–Pearson 95% CI 0.0–33.6%), whereas 5 of 24 pregnancies in the non-abstinence arm had a low-lying placenta (20.8%, 95% CI 7.1–42.2%). The two-sided Fisher's exact test comparing these proportions yielded p = 0.29. The absolute risk difference (abstinence minus non-abstinence) was −20.8 percentage points (95% CI −42.2 to +26.5). These point estimates suggest a lower incidence of low-lying placenta in the abstinence group, but the confidence intervals are wide and event counts small, so the results should be interpreted with caution. Detailed counts, proportions, 95% confidence intervals and exact p-values for the primary and key secondary outcomes are presented in Table 2

**Table 2 Primary and key secondary outcomes. It uses exact methods (Clopper–Pearson CIs, Fisher's exact p), and the numbers are your actual data.**

| Outcome | Abstinence (n=9) | Non-abstinence (n=24) | Absolute difference (95% CI) | Fisher's exact p |
|---|---|---|---|---|
| **Low-lying placenta** | 0/9 (0.0%), 95% CI 0.0–33.6% | 5/24 (20.8%), 95% CI 7.1–42.2% | −20.8% (−42.2 to +26.5) | 0.29 |
| **Preterm delivery (<37 wk)** | 1/9 (11.1%), 95% CI 0.3–48.3% | 1/24 (4.2%), 95% CI 0.1–21.1% | 6.9% (−16.8 to +39.0) | 0.56 |
| **Fetal growth restriction (FGR)** | 0/9 (0.0%), 95% CI 0.0–33.6% | 1/24 (4.2%), 95% CI 0.1–21.1% | −4.2% (−21.3 to +13.0) | 1.00 |
| **Preeclampsia (PE)** | 0/9 (0.0%), 95% CI 0.0–33.6% | 0/24 (0.0%), 95% CI 0.0–14.3% | 0.0% (−14.3 to +33.6) | 1.00 |
| **Placenta previa** | 0/9 (0.0%), 95% CI 0.0–33.6% | 0/24 (0.0%), 95% CI 0.0–14.3% | 0.0% (−14.3 to +33.6) | 1.00 |
| **NICU admission** | 1/9 (11.1%), 95% CI 0.3–48.3% | 0/24 (0.0%), 95% CI 0.0–14.3% | 11.1% (−11.1 to +39.6) | 0.27 |
| **Apgar <7 at 5 min** | 0/9 (0.0%), 95% CI 0.0–33.6% | 1/24 (4.2%), 95% CI 0.1–21.1% | −4.2% (−21.3 to +13.0) | 1.00 |
| **Major neonatal anomalies** | 0/9 (0.0%), 95% CI 0.0–33.6% | 0/24 (0.0%), 95% CI 0.0–14.3% | 0.0% (−14.3 to +33.6) | 1.00 |

Proportions displayed with Clopper–Pearson 95% CIs. Absolute difference = Abstinence − Non-abstinence (Newcombe-style approximate 95% CI). Fisher's exact two-sided p-values due to small counts. Because event counts are small, the comparisons are exploratory and imprecise.

**Per-protocol analysis.** All analysed pregnancies (n = 33) reported full adherence to the assigned peri-implantation behaviour and therefore the per-protocol analysis is identical to the mITT pregnancy analysis. Early low-lying placenta occurred in 0/9 (0.0%; Clopper–Pearson 95% CI 0.0–33.6%) pregnancies in the abstinence arm versus 5/24 (20.8%; 95% CI 7.1–42.2%) in the non-abstinence arm (Fisher's exact two-sided p = 0.290). The absolute risk difference (abstinence minus non-abstinence) was −20.8 percentage points (Newcombe 95% CI −40.5 to +11.2). Because adherence was self-reported, these per-protocol results should be interpreted cautiously.

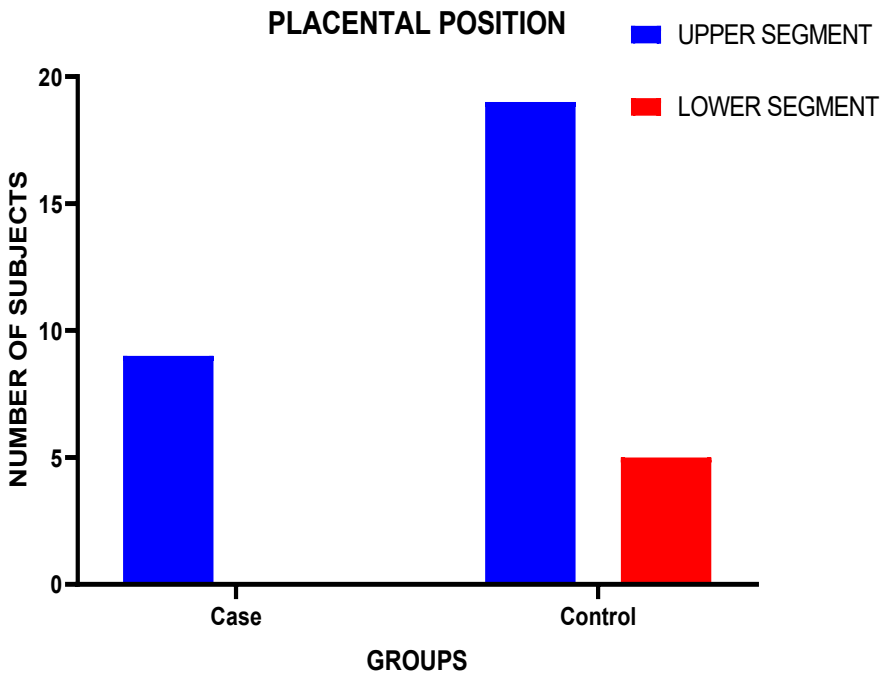


***Figure 2 A bar-chart showing the distribution of placental positions:*** **(PUS, AUS, Fundus, LP) in abstinence and non-abstinence groups. The abstinence group exhibited uniform placental positions in the posterior upper segment, while the non-abstinence group displayed greater variability, including 20.83% lower segment positions.**

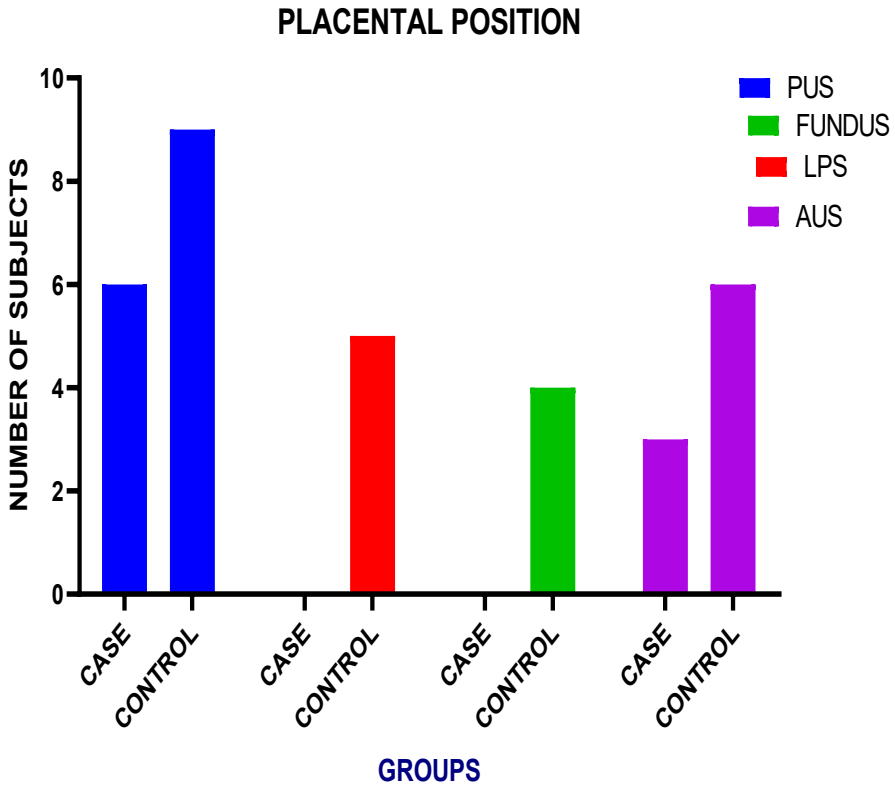


**Figure 3 A bar-chart showing the distribution of placental positions**

**To compare maternal and fetal outcomes between peri-implantation sexual abstinence and non-abstinence groups.**

Maternal outcomes analyzed included preeclampsia (PE), placenta previa, fetal growth restriction (FGR), and preterm delivery. Fetal outcomes included Apgar scores, NICU admissions, and neonatal anomalies, which are summarized in Table 2. There were no cases of preeclampsia or placenta previa in either arm. Fetal growth restriction was observed in one pregnancy in the non-abstinence arm (1/24, 4.2%) and in none of the nine pregnancies in the abstinence arm; the difference was not statistically significant (Fisher's exact p = 1.00) and confidence intervals are wide. Preterm delivery occurred once in each arm (1/9, 11.1% vs 1/24, 4.2%; Fisher's exact p = 0.56). Neonatal outcomes are shown in Table 4. One neonate in the abstinence arm required NICU admission following preterm delivery; there was a single Apgar score <7 in the non-abstinence arm (1/24, 4.2%), and no major neonatal anomalies in either group. The between-group comparisons for these infrequent events yielded non-significant Fisher p-values (all $p \geq 0.27$) and the associated confidence intervals are wide, reflecting the small number of pregnancies analysed.

## 6. DISCUSSION

In this randomized controlled trial of peri-implantation sexual abstinence, the abstinence arm had no cases of early low-lying placenta (0/9) compared with 5/24 (20.8%) in the non-abstinence arm. The two-sided Fisher's exact test for the primary comparison yielded p = 0.29; the absolute risk difference (abstinence − non-abstinence) was −20.8 percentage points (95% CI −42.2 to +26.5). Secondary maternal and neonatal events were infrequent and did not differ significantly between groups. Taken together, the data generate a signal, a lower point estimate of early low-lying placentation after peri-implantation abstinence, but the confidence intervals are wide and do not exclude clinically important benefit or harm. Thus, these findings should be considered hypothesis-generating rather than definitive.

### Placental Positioning and Clinical Implications

The position of the placenta is a critical determinant of pregnancy success, with low-lying placentas associated with complications such as placenta previa, hemorrhage, and preterm birth (13–15,17). In this study, the abstinence group exhibited a 0% incidence of low-lying placenta, compared to 20.8% in the non-abstinence group. Although this difference did not reach statistical significance ($p$=0.29), the trend aligns with emerging research on the mechanisms of implantation and placental development.

Upper-segment placental positioning (posterior upper segment [PUS], anterior upper segment [AUS], and fundus) is anatomically favorable due to the rich vascular supply and reduced mechanical stress in these regions (15). The position of the placenta is a critical determinant of pregnancy outcomes, it can influence pregnancy development, but interpreting early low-lying positioning as clinically significant requires caution, given that most cases resolve naturally through "placental migration." In one large cohort, 98.4% of mid-trimester low-lying placentas ascended to a normal position by delivery, with 95.9% resolved by 36 weeks (29). In our study, no low-lying placentas were observed in the abstinence group, compared to 20.8% in the non-abstinence group. Although this difference did not reach statistical significance (p = 0.29), it suggests a biological trend rather than a confirmed clinical effect, especially given the known potential for upward placental migration (29).

Implantation into the upper uterine segment (fundal, anterior, or posterior) may be anatomically favourable due to richer vascular supply and reduced mechanical stress (30).

The uniform upper-segment positioning seen in the abstinence group, contrasted with the variability in the non-abstinence group, is intriguing. However, it remains an exploratory finding that must be interpreted within the context of physiological migration, not as a definitive precursor to pathological outcomes like placenta previa multicenter studies to validate these findings

### Comparison of Maternal and Fetal Outcomes

Maternal and fetal outcomes are essential for assessing pregnancy success and complications. This study analyzed preeclampsia (PE), placenta previa, fetal growth restriction (FGR), preterm delivery, Apgar scores, NICU admissions, and neonatal anomalies. No cases of PE or placenta previa occurred. One FGR case was observed in the non-abstinence group, often linked to placental dysfunction. Preterm delivery occurred once in each group (11.1% vs 4.2%). A single NICU admission occurred in the abstinence group due to preterm birth, illustrating the multifactorial nature of adverse outcomes. Larger studies are needed to determine whether peri-implantation sexual abstinence measurably affects neonatal health.

### Potential Mechanisms Linking Sexual Activity and Implantation

Several biological mechanisms may explain the observed association between peri-implantation sexual activity and placental positioning. First, seminal fluid contains prostaglandins and cytokines (e.g., TGF-β, IL-6) that modulate endometrial receptivity (25,31). While these factors play a role in immune tolerance, excessive or dysregulated inflammation during the peri-implantation window could disrupt trophoblast invasion and placental anchoring (20,23,24,32). Second, orgasm-induced uterine contractions may mechanically displace the blastocyst, increasing the likelihood of implantation in the lower uterine segment (6). This hypothesis is supported by in vitro models demonstrating that shear stress impairs trophoblast migration and invasion (1,11). Finally, oxidative stress induced by seminal fluid components may further compromise

implantation. Elevated reactive oxygen species (ROS) during early pregnancy have been linked to impaired trophoblast function and shallow placental invasion (33,34). Together, these mechanisms suggest that sexual activity during the peri-implantation period could inadvertently create a suboptimal uterine environment for implantation.

**Strengths and Limitations**

This study's main strength is its randomized design with prospective follow-up from peri-implantation through delivery. Placental position was a prespecified outcome, assessed by ultrasound with stored images available for central review. Exact effect estimates and conservative statistical tests were applied, appropriate for small event counts.

Limitations include substantial pre-conception attrition, leaving only 33 pregnancies for the primary analysis and wide confidence intervals. Adherence to abstinence was self-reported, introducing potential recall and social desirability bias. The single-centre design may limit generalisability, and the small sample size restricted power to detect rare outcomes (e.g., placenta previa). Lack of biomarker data (e.g., seminal cytokines, uterine receptivity markers) also limited mechanistic insight.

Future research should test these findings in larger multicentre RCTs incorporating biomarker assays and possibly animal models to clarify biological pathways.

**Implications for practice and research**

The observed between-group difference in early low-lying placentation is intriguing but insufficient to change practice. Before any clinical recommendations on peri-implantation sexual behaviour can be made, replication in larger, prospectively registered randomized trials is necessary. Based on the observed event rates in this study (control low-lying placenta 20.8%, intervention 0.0%), a conventional sample-size calculation (two-sided $\alpha = 0.05$, 80% power, 1:1 allocation) requires approximately 33 pregnancies per arm (≈66 pregnancies total) to detect the observed absolute difference. Given our observed conversion from randomized couples to analyzed pregnancies (33 pregnancies from 94 enrolled; ~35% pregnancy yield), achieving 66 pregnancies would require enrolling on the order of 180–200 couples (estimate ≈ 66 / 0.35 ≈ 188). Investigators planning a definitive trial should therefore account for pre-conception attrition when choosing recruitment targets and consider multicentre recruitment to expedite enrollment and increase generalisability.

## 7. CONCLUSION

This randomized trial provides preliminary evidence that peri-implantation sexual abstinence may influence early placental positioning. No low-lying placentas were observed in the abstinence arm versus 20.8% in the non-abstinence arm, though the difference was not statistically significant and confidence intervals were wide due to limited sample size. Because most early low-lying placentas resolve spontaneously, the observed difference may represent a biological signal rather than a definitive clinical effect.

Despite these limitations, this study offers the first randomized evidence on a modifiable behavioral factor in implantation biology and placental development. Larger multicentre RCTs with objective adherence measures and mechanistic biomarker studies are needed to establish causality and clarify potential impacts on maternal–fetal outcomes.

**Declarations**

Ethics Approval and Consent to Participate

This study was approved by the USM Research Ethics Committee (JEPeM Code: USM/JEPeM/21030234). Written informed consent was obtained from all participants prior to enrolment, ensuring voluntary participation with the right to withdraw at any time. To uphold confidentiality, placental tissue samples were anonymised using unique code numbers and securely stored for up to three years for further analysis.

Consent for Publication

Not applicable. This manuscript does not contain identifying images or personal clinical details that could compromise participant anonymity.

Availability of Data and Materials

The datasets used and/or analysed during this study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

This research was funded by the Ministry of Higher Education, Malaysia, under the Fundamental Research Grant Scheme (FRGS/1/2020/SKK01/USM/02/3).

Authors' Contributions

Conceptualization and study design: Nik Ahmad Zuky Nik Lah, Abubakar Ibrahim, and Nik Hazlina Nik Hussain.

Funding Acquisition and Ethical Approvals: Nik Ahmad Zuky

Patient Recruitment and Data Collection: Abubakar Ibrahim and Engku Husna Engku Ismail, Nik Syamim Firdaus Nik Ahmad Zuky

Intervention and Trial Execution: Nik Ahmad Zuky and Sarimah Abdullah

Laboratory Analysis and Biomaker Assessment: Abubakar Ibrahim, Martina Irwan Khoo, Yusuf Lukman, Nik Syamim Firdaus Nik Ahmad Zuky, Anani Aila Mat Zin and Liza Noordin

Data Management & Statistical analysis: Abubakar Ibrahim, Engku Husna Engku Ismail, Yusuf Lukman and Sarimah Abdullah

Manuscript writing and Editing: Abubakar Ibrahim, Liza Noordin, Zaleha Abdullah Mahdy and Nik Ahmad Zuky

Final approval and manuscript review: Abubakar Ibrahim, Martina Irwan Khoo, Engku Husna Engku Ismail, Anani Aila Mat Zin, Liza Noordin, Sarimah Abdullah, Nik Syamim Firdaus Nik Ahmad Zuky, Nik Hazlina Nik Hussain, Zaleha Abdullah Mahdy and Nik Ahmad Zuky Nik Lah.

## REFERENCES

[1] Moreno I, Capalbo A, Mas A, Garrido-Gomez T, Roson B, Poli M, et al. The human periconceptional maternal-embryonic space in health and disease. Physiol Rev. 2023 July 1;103(3):1965–2038.

[2] Wilcox AJ, Baird DD, Weinberg CR. Time of implantation of the conceptus and loss of pregnancy. N Engl J Med. 1999 June 10;340(23):1796–9.

[3] Kim SM, Kim JS. A Review of Mechanisms of Implantation. Dev Reprod. 2017 Dec;21(4):351–9.

[4] Zhang S, Lin H, Kong S, Wang S, Wang H, Wang H, et al. Physiological and molecular determinants of embryo implantation. Mol Aspects Med. 2013 Oct;34(5):939–80.

[5] Stanford JB, Hansen JL, Willis SK, Hu N, Thomas A. Peri-implantation intercourse does not lower fecundability. Hum Reprod Oxf Engl. 2020 Aug 5;35(9):2107–12.

[6] Steiner AZ, Pritchard DA, Young SL, Herring AH. Peri-implantation Intercourse Lowers Fecundability. Fertil Steril. 2014 July;102(1):178–82.

[7] Fox CA, Wolff HS, Baker JA. Measurement of intra-vaginal and intra-uterine pressures during human coitus by radio-telemetry. J Reprod Fertil. 1970 July;22(2):243–51.

[8] Kafaei Atrian M, Sadat Z, Rasolzadeh Bidgoly M, Abbaszadeh F, Asghari Jafarabadi M. The Association of Sexual Intercourse During Pregnancy With Labor Onset. Iran Red Crescent Med J. 2014 Dec 26;17(1):e16465.

[9] Wilcox. The timing of the “fertile window” in the menstrual cycle: day specific estimates from a prospective study | The BMJ [Internet]. 2000 [cited 2024 Dec 22]. Available from: https://www.bmj.com/content/321/7271/1259

[10] Ma M, Zhang L, Liu Z, Teng Y, Li M, Peng X, et al. Effect of blastocyst development on hatching and embryo implantation. Theriogenology. 2024 Jan 15;214:66–72.

[11] Zhou J, West RC, Ehlers EL, Ezashi T, Schulz LC, Roberts RM, et al. Modeling human peri-implantation placental development and function†. Biol Reprod. 2021 July 1;105(1):40–51.

[12] Lan VTN, Khang VN, Nhu GH, Tuong HM. Atosiban improves implantation and pregnancy rates in patients with repeated implantation failure. Reprod Biomed Online. 2012 Sept;25(3):254–60.

[13] Amer MB. Placental location in the uterus and its roles in fetal, maternal outcome and mode of delivery. Arch Venez Farmacol Ter. 2021;40(5):487–91.

[14] Babayan A, Hellmann R, Struk I, Roberts MC. The Effects of Placental Location on Maternal and Neonatal Outcomes: A Retrospective Cohort Study. J Diagn Med Sonogr. 2024 July 1;40(4):361–6.

[15] Doctory N, Romano A, Navon I, Barbash-Hazan S, Bardin R, Hadar E. Placental location and obstetrical-neonatal outcomes: A retrospective study. Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet. 2023 Feb;160(2):641–5.

[16] Anderson-Bagga FM, Sze A. Placenta Previa. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Apr 10]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK539818/

[17] Jansen CHJR, van Dijk CE, Kleinrouweler CE, Holzscherer JJ, Smits AC, Limpens JCEJM, et al. Risk of preterm birth for placenta previa or low-lying placenta and possible preventive interventions: A systematic review and meta-analysis. Front Endocrinol. 2022 Sept 2;13:921220.

[18] Jing L, Wei G, Mengfan S, Yanyan H. Effect of site of placentation on pregnancy outcomes in patients with placenta previa. PloS One. 2018;13(7):e0200252.

[19] King LJ, Dhanya Mackeen A, Nordberg C, Paglia MJ. Maternal risk factors associated with persistent placenta

previa. Placenta. 2020 Sept 15;99:189–92.

[20] Adefuye AO, Adeola HA, Sales KJ, Katz AA. Seminal Fluid-Mediated Inflammation in Physiology and Pathology of the Female Reproductive Tract. J Immunol Res. 2016;2016:9707252.

[21] Ahmadi H, Csabai T, Gorgey E, Rashidiani S, Parhizkar F, Aghebati-Maleki L. Composition and effects of seminal plasma in the female reproductive tracts on implantation of human embryos. Biomed Pharmacother. 2022 July 1;151:113065.

[22] Dj S, Kp T, Mj J, K GD, Sa R. Seminal fluid induces leukocyte recruitment and cytokine and chemokine mRNA expression in the human cervix after coitus. J Immunol Baltim Md 1950 [Internet]. 2012 Mar 1 [cited 2024 Oct 5];188(5). Available from: https://pubmed.ncbi.nlm.nih.gov/22271649/

[23] Robertson SA, Prins JR, Sharkey DJ, Moldenhauer LM. Seminal fluid and the generation of regulatory T cells for embryo implantation. Am J Reprod Immunol N Y N 1989. 2013 Apr;69(4):315–30.

[24] Saftlas AF, Rubenstein L, Prater K, Harland KK, Field E, Triche EW. Cumulative exposure to paternal seminal fluid prior to conception and subsequent risk of preeclampsia. J Reprod Immunol. 2014 Mar 1;101–102:104–10.

[25] Shen Q, Wu X, Chen J, He C, Wang Z, Zhou B, et al. Immune Regulation of Seminal Plasma on the Endometrial Microenvironment: Physiological and Pathological Conditions. Int J Mol Sci. 2023 Jan;24(19):14639.

[26] Favaro C, Pearson JT, Rowland SP, Jukic AM, Chelstowska M, Berglund Scherwitzl E, et al. Time to Pregnancy for Women Using a Fertility Awareness Based Mobile Application to Plan a Pregnancy. J Womens Health. 2021 Nov;30(11):1538–45.

[27] Pfeifer S, Butts S, Fossum G, Gracia C, La Barbera A, Mersereau J, et al. Optimizing natural fertility: a committee opinion. Fertil Steril. 2017 Jan 1;107(1):52–8.

[28] Hopewell S, Chan AW, Collins GS, Hróbjartsson A, Moher D, Schulz KF, et al. CONSORT 2025 statement: updated guideline for reporting randomised trials. 2025 Apr 14 [cited 2025 Sept 26]; Available from: https://www.bmj.com/content/389/bmj-2024-081123

[29] Heller HT, Mullen KM, Gordon RW, Reiss RE, Benson CB. Outcomes of Pregnancies With a Low-Lying Placenta Diagnosed on Second-Trimester Sonography. J Ultrasound Med. 2014;33(4):691–6.

[30] Kükrer S, Arlıer S, Dilek O, Gülümser Ç. A novel approach for the early prediction and prevention of placenta accreta spectrum and severe peripartum hemorrhage in patients with complete placenta previa: leveraging three-dimensional placental topography, cervical length, and dilatation parameters on magnetic resonance imaging. BMC Pregnancy Childbirth. 2024 Nov 25;24(1):784.

[31] Bromfield JJ. Seminal fluid and reproduction: much more than previously thought. J Assist Reprod Genet. 2014 June;31(6):627–36.

[32] Robertson SA, Guerin LR, Bromfield JJ, Branson KM, Ahlström AC, Care AS. Seminal Fluid Drives Expansion of the CD4+CD25+ T Regulatory Cell Pool and Induces Tolerance to Paternal Alloantigens in Mice1. Biol Reprod. 2009 May 1;80(5):1036–45.

[33] Mukherjee I, Dhar R, Singh S, Sharma JB, Nag TC, Mridha AR, et al. Oxidative stress-induced impairment of trophoblast function causes preeclampsia through the unfolded protein response pathway. Sci Rep. 2021 Sept 16;11(1):18415.

[34] Zhang C, Guo Y, Yang Y, Du Z, Fan Y, Zhao Y, et al. Oxidative stress on vessels at the maternal-fetal interface for female reproductive system disorders: Update. Front Endocrinol [Internet]. 2023 Mar 10 [cited 2024 Dec 17];14. Available from: https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2023.1118121/full.