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Original article

Menstrual cycle characteristics and fecundability in a North American preconception cohort

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ABSTRACT

Purpose: The aim of this study was to evaluate the association between menstrual cycle characteristics in early life and adulthood and fecundability.
Methods: Pregnancy Study Online (PRESTO) is an Internet-based preconception cohort study of pregnancy planners from the United States and Canada. During the preconception period, we enrolled 2189 female pregnancy planners aged 21–45 years who had been attempting conception for ≤6 cycles. Women self-reported menstrual cycle characteristics via an online baseline questionnaire, and pregnancy status was ascertained through bimonthly follow-up questionnaires. Proportional probabilities models were used to estimate fecundability ratios (FRs) and 95% confidence intervals (CIs), adjusting for potential confounders.
Results: Compared with usual menstrual cycle lengths of 27–29 days, cycle lengths of <25 (FR = 0.81, 95% CI: 0.54–1.22) and 25–26 days (FR = 0.92, 95% CI: 0.75–1.14) were associated with reduced fecundability. Compared with women who reached menarche at the age of 12–13 years, those who reached menarche at <12 years had reduced fecundability (FR = 0.87, 95% CI: 0.76–0.99). Women whose cycles never regularized after menarche (FR = 0.93, 95% CI: 0.81–1.06) had slightly reduced fecundability compared with women whose cycles regularized within 2 years of menarche. Bleed length and heaviness of bleeding were not appreciably associated with fecundability.
Conclusions: Menstrual cycle characteristics, specifically cycle length and age at menarche, may act as markers of fertility potential among pregnancy planners.

Introduction

The menstrual cycle is characterized by a series of feedback responsive processes in the hypothalamic–pituitary–ovarian axis. These changes allow for the release of a mature egg from the dominant ovarian follicle and the development of a receptive endometrial lining that can support a pregnancy [1]. Menstrual patterns are a marker of ovarian and hormonal function and may be related to fecundity, the biologic capacity for reproduction [2]. Women with irregular cycles may have longer time to pregnancy due to higher risk of anovulation [2], an underlying disorder of the hypothalamic–pituitary–ovarian axis or the uterus [3], and/or difficulty timing intercourse to the fertile window [4].

Several studies support an association between cycle length and fecundity, even after controlling for age. Short cycles may reflect ovarian aging [5] or a narrow fertile window and are associated with higher risk of anovulation [2] and lower fecundability compared with normal length cycles [6–8]. However, evidence assessing the association between long menstrual cycles and fecundability is inconsistent. In an in vitro fertilization (IVF) cohort, egg donors with regular menstrual cycles of 34–35 days had lower gonadotropin medication requirements, improved oocyte quality, and better cycle success compared with donors with menstrual cycles of 27–28 days [9]. Cycle length has been positively associated

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with pregnancy rates in women undergoing IVF [10] and with improved fecundability among pregnancy planners [6] but also with increased risk of anovulation [2] and reduced fecundability [7,8]. Long irregular cycles may reflect underlying gynecologic disease, and inconsistencies in prior studies may relate to varying exclusion criteria (e.g., women with irregular cycles or women whose menstrual characteristics are obscured by recent hormone use). Differing study designs and small study sizes may also account for inconsistencies in the literature.

Bleed length and heaviness of bleeding may act as markers of endometrial development. In a study of regularly menstruating, healthy females in the United States, anovulatory cycles were followed by lighter blood loss and shorter bleed length compared with ovulatory cycles [11]. These findings are supported by other prospective cohort studies that have found an association between short cycle length and lower fertility [7,12]. However, a Danish preconception cohort study found only slightly lower fecundability among women with short bleeds or light menstrual flow [6].

In a cohort of North American pregnancy planners, we examined early life menstrual cycle characteristics (age at menarche and time until cycle regularity) and current menstrual cycle characteristics (irregular cycles, cycle length, bleed length, and heaviness of bleed) in relation to fecundability.

Materials and methods

Study population

Pregnancy Study Online (PRESTO) is an Internet-based preconception cohort study of pregnancy planners in the United States and Canada. The study methodology has been described in detail elsewhere [13]. Recruitment began in June 2013 and was conducted primarily through banner advertisements on social media and health-related websites. Eligible women were aged 21–45 years, in a stable relationship with a male partner, and not using contraception or fertility treatments. The Institutional Review Board of Boston University Medical Center approved the study protocol, and all participants provided informed consent.

Study procedures

Participants completed an online baseline questionnaire on demographics, medical history, and lifestyle habits, followed by shorter online questionnaires every 8 weeks for up to 12 months or until reported conception. Follow-up questionnaires collected updated exposure information and ascertained pregnancy status. Over 80% of women completed at least one follow-up questionnaire [13].

Women who completed the baseline questionnaire were randomized with 50% probability to receive a complimentary premium subscription to Fertility Friend (FF), a menstrual cycle charting and fertility information software program. FF users record daily information on the presence and heaviness of menstrual bleeding. They receive email tutorials from FF on monitoring their fertility and using different features of the software program but were not provided with additional encouragement or incentives to use FF.

Assessment of menstrual cycle characteristics

Participants reported the age when they experienced their first menstrual period on the baseline questionnaire. To assess time from menarche until cycle regularity, we asked, “Did your period become regular on its own without the use of hormonal contraceptives …?” Women who responded “no” were classified as “never regular”. Women who responded “cannot say because I was taking hormones most of the time” were classified as “hormone-obscured.” Women who responded “yes” were asked to report the age when their periods became regular. We calculated time until cycle regularity as the difference between age at menarche and age when periods became regular.

On the baseline questionnaire, we asked participants if their menstrual periods were regular in the past couple of years when not using hormonal contraceptives (“regular so you can usually predict about when your next period will begin”). If a woman reported regular cycles, she was asked to report her typical menstrual cycle length when not using contraception, defined as the number of days from the first day of one menstrual period to the first day of the next menstrual period. For women with missing or implausible responses to this question (3.4% of regularly-cycling women who were not long-term hormone users), we used data from follow-up questionnaires (self-reported cycle length or difference in last menstrual period (LMP) dates) to calculate cycle length. We also asked participants about their typical bleed length (defined as the number of days of bleeding, not spotting) and total amount of menstrual flow (light: $\leq$10 pads/tampons per menses, moderate: 11–20 pads/tampons per menses, moderate/heavy: 21–30 pads/tampons per menses, and heavy: $>$30 pads/tampons per menses).

Validation of menstrual cycle characteristics

We used the subset of women who provided prospective daily FF data to validate cycle length and bleed length reported on the baseline questionnaire. To calculate cycle length from FF data, we identified the first day of bleeding (not including spotting) that was immediately preceded by a day of spotting or no bleeding for each cycle and took the difference in the first dates of each pair of consecutive cycles. We averaged cycle length across all prospectively reported cycles in FF for each woman and compared it with cycle length reported at baseline.

We identified the first day of each menstrual cycle, as defined previously, and the last day of each bleed, defined as a day of bleeding followed by a day of nonbleeding, and took the difference in these days to calculate bleed length. We averaged bleed length across all prospectively reported cycles in FF for each woman and compared it with bleed length reported at baseline.

Assessment of covariates

Women reported data on age, race, ethnicity, education, income, height, weight, physical activity, parity, perceived stress scale (PSS-10) [14], multivitamin or folic acid intake, smoking, alcohol and caffeine intake, intercourse frequency, last method of contraception at baseline, and history of polycystic ovarian syndrome, endometriosis, and uterine leiomyomata (fibroids) diagnoses. We updated information on frequency of intercourse over time using data from the follow-up questionnaires.

Assessment of pregnancy and cycles at risk

On each follow-up questionnaire, participants reported the date of their LMP and whether they had conceived since their last follow-up. We calculated total cycles at risk from the number of cycles attempting conception at study entry, date of LMP before enrollment, usual cycle length, and LMP date on each follow-up questionnaire. Participants contributed cycles to the analysis from enrollment until conception, initiation of fertility treatment, loss to follow-up, or 12 months, whichever came first.