Original article

Pregnancy loss history at first parity and selected adverse pregnancy outcomes

Katherine A. Ahrens PhD [a,*], Lauren M. Rossen PhD [a], Amy M. Branum PhD [b]

[a] Infant, Child, and Women's Health Statistics Branch, Office of Analysis and Epidemiology, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD
[b] Reproductive Statistics Branch, Division of Vital Statistics, National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, MD

A B S T R A C T

Purpose: To evaluate the association between pregnancy loss history and adverse pregnancy outcomes.
Methods: Pregnancy history was captured during a computer-assisted personal interview for 21,277 women surveyed in the National Survey of Family Growth (1995–2013). History of pregnancy loss (<20 weeks) at first parity was categorized in three ways: number of losses, maximum gestational age of loss(es), and recency of last pregnancy loss. We estimated risk ratios for a composite measure of selected adverse pregnancy outcomes (preterm, stillbirth, or low birthweight) at first parity and in any future pregnancy, separately, using predicted margins from adjusted logistic regression models.
Results: At first parity, compared with having no loss, having 3+ previous pregnancy losses (adjusted risk ratio (aRR) = 1.66 [95% CI = 1.13, 2.43]), a maximum gestational age of loss(es) at ≥10 weeks (aRR = 1.28 [1.04, 1.56]) or having experienced a loss 24+ months ago (aRR = 1.36 [1.10, 1.68]) were associated with increased risks of adverse pregnancy outcomes. For future pregnancies, only having a history of 3+ previous pregnancy losses at first parity was associated with increased risks (aRR = 1.97 [1.08, 3.60]).
Conclusion: Number, gestational age, and recency of pregnancy loss at first parity were associated with adverse pregnancy outcomes in U.S. women.

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Introduction

Although pregnancy loss is a common occurrence [1,2], questions regarding its etiology and association with other reproductive outcomes remain unanswered. While associations between recurrent pregnancy loss and preterm birth in the subsequent pregnancy have been recognized for decades [3–5], the associations between nonrecurrent loss, gestational age of loss, and recency of loss and the risks of other adverse pregnancy outcomes are less clear. In part, this may be due to choice of comparison group; for example, comparing women with only pregnancy loss to women with a history of live birth may lead to inflated risk estimates associated with pregnancy loss [5–8].

Only a handful of studies have examined history of nonrecurrent pregnancy loss on risk of adverse pregnancy outcomes at subsequent pregnancy among primiparous women [7–15]. These studies have been limited by a small number of study participants [11], restriction to pregnancy losses requiring a hospital visit [8,12], or by sparse reproductive history information, including lack of data on gestational age of loss, how long ago the loss occurred, and history of induced abortions [7,9,10,13–15]. In addition, prior studies have only considered the outcome of the pregnancy subsequent to the loss and not other future pregnancies the primiparous women will experience.

The objective of our study was to estimate the risks of preterm birth, stillbirth, low birthweight, and a composite outcome of any of the above conditions by pregnancy loss history at first parity among reproductive aged women in the United States.

Material and methods

Study population

The National Survey of Family Growth (NSFG) is a cross-sectional survey conducted by the Centers for Disease Control and Prevention's National Center for Health Statistics [16]. We included data from female respondents from four survey periods: 1995, 2002, 2006—2010, and 2011—2013. Each survey period includes a multistage, probability-based, nationally representative sample of the household population aged 15—44 years. The National Center for Health Statistics Research Ethics Review Board approved each of these NSFG data collection efforts, and no specific additional review was required for this data analysis.

Pregnancy loss history

Female respondents provided a complete pregnancy history during a computer-assisted in-person interview. Pregnancy history included, for each pregnancy, the calendar month and year at end of pregnancy, the gestational length and the pregnancy outcome (e.g., miscarriage, stillbirth, abortion, ectopic pregnancy, live birth) [17]. We defined pregnancy loss as a self-reported "miscarriage" with a gestational length <20 weeks [18].

Three aspects of pregnancy loss were assessed in separate analyses: number of losses (no loss, 1, 2, 3, or more), gestational age of pregnancy loss(es) (all <6 weeks, longest 6—9 weeks, longest ≥10 weeks), and recency of the last pregnancy loss (interpregnancy interval <6 months, 6 to 11 months, 12 to 23 months, 24 months or more [9]). In addition, we defined pregnancy loss dichotomously (no loss, at least 1). Cutpoints for gestational age of pregnancy loss(es) were based on the assumed development stage of the conceptus given the time of pregnancy loss recognition, with losses before 6 weeks representing pre-embryologic losses, 6 to 9 weeks representing embryo losses, and ≥10 weeks representing fetal losses [18,19]. Losses before 6 weeks are alternatively defined as "early pregnancy loss" and can represent pre-clinical pregnancy losses [2,20].

Adverse pregnancy outcomes

For each completed pregnancy, the following adverse pregnancy outcomes were identified: preterm birth (live birth at <37 weeks' gestation), stillbirth (self-reported "stillbirth" or pregnancy loss at 20 weeks' gestation or greater), and low birthweight (live birth <2500 g). In addition, a composite measure, indicating if any of the above adverse pregnancy outcome occurred, was created.

Study participant characteristics

We examined the following participant characteristics using information collected during the NSFG interview: age at conception, height, marital status at the end of each pregnancy, Hispanic origin and race, intendedness of each pregnancy at conception, number of live births from each pregnancy, any use of medical help to become pregnant ever, ever smoked, highest educational attainment and family income as percentage of poverty level at the time of the interview. We defined a yes/no variable for any history of induced abortion at the beginning of each pregnancy.

Statistical analysis

Our analysis used the first pregnancy resulting in a live birth or stillbirth, hereafter referred to as "first parity", as the time point for defining pregnancy loss history. We focused on first parity to minimize selection bias introduced by only including women who, through choice or fecundity, achieved at least two pregnancies proceeding past 20 weeks. First parity has also been increasingly preferred as the analytical cohort to study the association between pregnancy loss and subsequent pregnancy outcomes to control for confounding by prior live birth [7—15]. We examined (1) the pregnancy outcome of the first parity and (2) the collapsed pregnancy outcomes of all pregnancies after first parity (hereafter referred to as "future pregnancies") reported at the time of interview.

Number of pregnancy losses at first parity was tabulated across participant characteristics (see supplemental tables 1 and 2 for tabulations of the two other aspects of pregnancy loss). Using χ^2 tests, comparisons were made between women with no loss versus at least one loss and, for comparing aspects of pregnancy loss against each other, among only women with losses.

Risks of preterm birth, stillbirth, low birthweight, the composite measure, and mean gestational length of pregnancy were tabulated by pregnancy loss history at first parity. For the future pregnancies analysis, we restricted the data set to women who reported at least one additional pregnancy. We present the proportions of women with any future pregnancy, live birth, miscarriage, induced termination, and ectopic pregnancy in a supplemental table 3.

Risk ratios (RRs) and 95% confidence intervals (CIs) for the composite outcome measure at first parity and among any future pregnancy(ies) were estimated, separately, using predicted margins from logistic regression. Models were adjusted for factors associated with either preterm birth, stillbirth, or low birthweight [21—23] and included all the participant characteristics previously described except intendedness of pregnancy at conception and multiple live births at first parity, time-varying factors which could fall along the causal pathway from pregnancy loss to future pregnancy outcome. We assessed the significance of adding an interaction term for year of conception to evaluate if the relationship between pregnancy loss history and adverse pregnancy outcomes might be heterogeneous over time. A previous study using NSFG pregnancy data found the incidence of pregnancy loss appeared to be increasing by about 1.0% per year from 1970 to 2000 [24], which could indicate changes in the relationship between pregnancy loss and adverse pregnancy outcomes over time.

Analyses were conducted with SAS, 9.3 (SAS Institute, Cary, North Carolina), SUDAAN, 11.0 (RTI International, Research Triangle Park, North Carolina) or STATA, SE 13 (StataCorp LP, College Station, TX) and took into account the complex survey design.

Results

Study population

There were 36,370 women aged 15 to 44 years who participated in NSFG cycles 1995, 2002, 2006—2010, and 2011—2013; 23,835 (64%, standard error [SE] = 0.5) women reported a total of 64,970 pregnancies, 21,277 of which were at first parity age 12 years and older. Reproductive history at the time of interview and at first parity was largely similar among survey periods (see supplemental table 4); however, the percent with at least one pregnancy loss at the time of first parity was higher in 2011—2013 compared with 1995 (13% vs. 10%, P < .01).

Pregnancy loss history

Among our study population, 88.8% (SE = 0.3) reported having no history of pregnancy loss at the time of first parity, 9.4%