Recurrent Pregnancy Loss

Evaluation and Treatment

Lora Shahine, MD[a,b], Ruth Lathi, MD[c,*]

KEYWORDS

- Recurrent pregnancy loss • Recurrent miscarriage • Recurrent fetal loss
- Recurrent embryonic loss

KEY POINTS

- Evaluation for women with recurrent pregnancy loss includes checking for uterine anomalies and parental chromosomal rearrangements and testing for antiphospholipid antibodies.
- Fifty percent of patients will have no definite cause for recurrent pregnancy loss after a thorough evaluation.
- The prognosis for a live birth in women with unexplained recurrent pregnancy loss is 50% to 80% without intervention with evidence-based treatments and supportive care.
- More than half of first-trimester miscarriages tested will have sporadic numeric chromosomal abnormalities.
- Chromosomal screening of embryos after in vitro fertilization has been proposed as a treatment option to reduced aneuploidy conceptions, but it has not been evaluated in randomized controlled studies.

BACKGROUND AND DEFINITIONS

The definitions of miscarriage and recurrent pregnancy loss (RPL) are important to review because they vary within the literature and clinical teaching. Classically, RPL is defined as 3 pregnancy losses before the twentieth week of gestation and excludes ectopic, molar, and biochemical pregnancies. The American Society of Reproductive Medicine (ASRM) states that, for the purposes of determining whether an evaluation for RPL is appropriate, pregnancy is defined as a clinical pregnancy documented by ultrasonography or histopathologic examination and that a clinical evaluation may proceed following 2 first-trimester pregnancy losses.[1] ASRM

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[a] Pacific NW Fertility and IVF Specialists, Seattle, WA, USA; [b] Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Washington School of Medicine, Seattle, WA, USA; [c] Division of Reproductive Endocrinology and Infertility, Stanford University School of Medicine, Stanford, CA, USA
* Corresponding author.
E-mail address: rlathi@stanford.edu

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maintains that a threshold of 3 or more pregnancy losses should be used for epidemiologic studies.[1]

RPL may be considered a primary or secondary condition. Primary RPL refers to multiple pregnancy losses in which a patient has never had a live birth, and secondary RPL refers to multiple pregnancy losses in a patient who has had a live birth previously.[2] Definitions are provided in **Table 1**.

INCIDENCE

Clinically recognized pregnancy loss occurs in approximately 15% to 25% of all pregnancies.[1] If preclinical losses are included, pregnancy loss is estimated to be as high as 57%.[3–5] It is estimated that less than 5% of women will experience 2 consecutive pregnancy losses and that only 1% of women will experience 3 or more.[3] The incidence of miscarriage increases with age of the woman such that women less than 35 years old have a 9% to 12% risk of spontaneous loss in the first trimester,[4,5] but this risk increases to 50% in women aged 40 years and older.[5–7]

EVALUATION AND TREATMENT BY CAUSE

RPL has been associated with factors related to genetics, age, antiphospholipid syndrome, uterine anomalies, thrombophilias, hormonal or metabolic disorders, infection, autoimmunity, sperm parameters, and lifestyle issues. With a thorough evaluation, a definitive diagnosis for RPL will be made in only 50% of patients. The following review of causes includes the evidence-based evaluation for RPL associated with each cause.

ANATOMIC CAUSES

Congenital and acquired uterine anomalies are found in 10% to 15% of women with RPL compared with 7% of all reproductive-aged women.[8,9] A uterine evaluation is widely considered an important part of the evaluation for patients with RPL and may include a hysterosalpingogram (HSG), saline infusion sonogram (SIS), 3-dimensional (3D) ultrasound, diagnostic hysteroscopy, or MRI.

Congenital uterine anomalies are associated with second-trimester losses and other obstetric complications, such as preterm labor, fetal malpresentation, and a higher rate of delivery by cesarean section. Although the role of uterine anomalies in

Table 1
Definitions of pregnancy and RPL

Pregnancy	Clinical pregnancy documented by ultrasonography or histopathologic examination
Clinical miscarriage	Pregnancy loss before the twentieth week of gestation
Biochemical pregnancy	Beta Human Chorionic Gonadotropin hormone detected in urine or blood stream, but pregnancy loss occurs before it could be clinically documented
RPL: classic definition	Three pregnancy losses before the twentieth week of gestation and excludes ectopic, molar, and biochemical pregnancies
RPL: evaluation indicated according to ASRM	Clinical evaluation may proceed following 2 first-trimester pregnancy losses
Primary RPL	RPL in a patient who has never had a live birth
Secondary RPL	RPL in a patient who has had at least one live birth