Primary ovarian insufficiency: a glimpse into the racial and socioeconomic disparities found within third-party reproduction

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Objective: To describe a unique case of primary ovarian insufficiency and review the systemic barriers in place that hinder reproductive autonomy for Black women who require third-party reproduction.
Design: Case report and review of the literature.
Setting: Safety-net hospital in an urban community.
Patient(s): A 36-year-old Black woman, gravida 0, with primary ovarian insufficiency who desires future fertility but is restricted by systemic barriers.
Intervention(s): Chromosome analysis.
Main Outcome Measure(s): Not applicable.
Result(s): Balanced reciprocal translocation between chromosomes 1 and 13: 46,XX,t(1;13)(q25;q14.1).
Conclusion(s): The field of assisted reproductive technology has evolved at an exponential rate, yet it unfortunately benefits some and not all. It is imperative that when we advocate for full spectrum infertility care, that this encompasses everyone. As we continue to further study and develop assisted reproductive technology, we must not forget to consider the factors leading to racial and socioeconomic disparities in reproductive care access, utilization, and outcomes. (Fertil Steril Rep® 2022;3:62–5. ©2021 by American Society for Reproductive Medicine.)
Key Words: Infertility, disparity, gamete, donor, ethnicity

INTRODUCTION

Primary ovarian insufficiency (POI) is a condition characterized by oocyte depletion before 40 years of age, resulting in the development of hypergonadotropic hypogonadism. The resultant hypoestrogenemia inhibits the negative feedback system within the hypothalamic–pituitary–ovarian axis, thus significantly raising serum gonadotropin levels. Although POI typically manifests along a spectrum, the most severe form presents with infertility, amenorrhea, and vasomotor symptoms. Concomitant health concerns of prolonged undertreated hypoestrogenemia include decreased bone mineral density and cardiovascular morbidity (1).

Primary ovarian insufficiency can be categorized as spontaneous or iatrogenic (i.e., resulting from surgical oophorectomy or gonadotoxic therapy). The incidence of spontaneous POI is estimated to be approximately 1% of women aged <40 years and 0.1% of women aged <30 years (1). Few epidemiological studies in the literature investigate the prevalence of POI among different racial/ethnic groups. Luborsky et al. (2) sought to determine the racial prevalence of POI in a cross-sectional survey that was used to determine eligibility for participation in the Study of Women's Health Across the Nation. This study included over 15,000 participants (7,771 Caucasian, 4,393 Black, 1,942 Hispanic, 654 Chinese, and 845 Japanese) across multiple clinical sites. Primary ovarian

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insufficiency was found in 1% of Caucasian, 1.4% of Hispanic, 1.4% of African American, 0.5% of Chinese, and 0.1 % of Japanese women (2).

Although most commonly deemed as idiopathic, specific etiologies of spontaneous POI include genetic abnormalities, autoimmune conditions, and infections (1, 3). Genetic etiologies of POI are most commonly due to abnormalities involving the X chromosome and rarely are associated with autosomal mutations (3).

Here, we report a case of POI associated with a balanced autosomal translocation as well as the systemic barriers in place that attenuate this patient's ability to reach her fertility goals. Informed consent was obtained from the patient for publication of this case report, which was documented by a third-party witness in the electronic medical record. No identifiable or protected health information is presented. Additionally, we provide a brief review of the literature on health disparities in access, utilization, and outcomes of infertility care and third-party reproduction.

CASE REPORT

A 36-year-old G0 self-identified Black woman presented to a safety-net hospital in an urban community with a 5-month history of secondary amenorrhea, after 2.5 years of oligomenorrhea. She denied hot flashes, vaginal dryness, malignancy, chemotherapy/radiation exposure, or autoimmune disease. Her past medical history was notable for recently diagnosed stage 4 chronic kidney disease requiring dialysis, hyperparathyroidism, hypertension, and osteoporosis. The patient was adopted, and her family history was unknown. The rest of her medical history was unremarkable.

On examination, her height and body mass index were 144.78 cm and 23.15 kg/m^2, respectively, and the remaining general physical examination findings were unremarkable. Laboratory results revealed a negative urine pregnancy test, serum follicle-stimulating hormone level of >400 mIU/mL (on two consecutive samples), estradiol level of 26 pg/mL, inhibin-B level of <10 pg/mL, and antimüllerian hormone level of <0.03 ng/mL. The serum prolactin and thyroid-stimulating hormone levels were within normal limits. Additionally, serum anti-21-hydroxylase, anti-double-stranded DNA, and anti-nuclear antibody were negative. On pelvic ultrasonography, the endometrial echo was 1.1 cm, bilateral ovaries were unidentifiable, and the rest of the pelvic anatomy was otherwise normal.

Chromosome analysis of peripheral blood lymphocytes revealed a balanced reciprocal translocation between the long arms of chromosomes 1 and 13: 46,XX,t(1;13)(q25;q14.1) in all metaphases at >550 G banding resolution.

The patient strongly desired future fertility and was referred to our Reproductive Endocrinology and Infertility service, where she was counseled on the improbable likelihood of natural spontaneous conception in the setting of POI. Furthermore, it was explained that autologous in vitro fertilization (IVF) would be ineffective. Thus, her only options for future parenthood would be adoption or utilization of donor gametes/embryo with or without a gestational carrier. None of these options were financially feasible for this patient.

DISCUSSION

Access to Specialized Fertility Care

A diagnosis of POI can be life-altering and devastating for any woman. Only 5%–10% of women with POI may have a spontaneous pregnancy and live birth after spontaneous intermittent ovulation (1). Fortunately, the technological advances made within the field of infertility have been nothing short of tremendous. Since its invention in the 1970s, IVF has evolved into the most efficacious treatment for infertility, curing millions of couples worldwide (4). Recent estimates show that over 8 million infants have been born from IVF, as of 2020 (5). However, as monumental as this may be, these technological advancements are tainted by race and class-based barriers to access (4).

In the United States (US), the average cost of one cycle of IVF exceeds $12,000 (4). When adding the costs of medications, anesthesia, and adjunctive therapies, such as intracytoplasmic sperm injection, blastocyst culture, and cryopreservation, the average total costs exceed $20,000. Preimplantation genetic testing incurs further costs. After years of advocacy, public outcries for policy change have led to 19 states having mandated some degree of fertility coverage, as of April 2021. The term "coverage," however, carries a slew of stipulations that differ for each state, from a maximum number of covered cycles to a minimum amount of treatment required before commencing IVF (6). Despite these advances, the vast majority of the US population remains without fertility coverage and, thus, without a viable avenue to build their families, should medical assistance be needed. Additionally, the aforementioned state mandates exclude federal insurance programs. Even the Affordable Care Act did little to tackle the financial barrier to access, as it excludes coverage of assisted reproductive technology (ART) treatments based on its interpretation of infertility as "non-life-threatening", thus deeming related procedures "elective" (4).

Regardless of "necessity," this system undoubtedly leads to a disparity in access and utilization for those of low socioeconomic status. This disproportionately affects ethnic minorities as well as other marginalized groups (7). Furthermore, the patient described in this case faces additional challenges in pursuit of conceiving due to her medical history. Patients with end-stage kidney disease and on dialysis face an increased risk of poor pregnancy outcomes, such as higher rates of preeclampsia, cesarean delivery, stillbirth (with 50% of fetal/infant loss), fetal growth restriction, and preterm birth. When patients on dialysis conceive, they also risk losing additional renal function (8, 9). Subsequently, the recommended options include adoption and third-party reproduction, specifically with a gestational carrier to improve the likelihood of optimal pregnancy outcomes. The unattainability of these options for this patient further complicates her treatment plan, exacerbating barriers while attenuating her chances of reaching her personal fertility goals.

Disparate ART Outcomes

As technological advances continue to progress over time, epidemiological studies in the US have demonstrated persistent racial/ethnic disparities in the prevalence of infertility as well as ART utilization and outcomes (7, 10–12). This was reconfirmed in 2021 by Jackson-Bey et al. (13) in a systematic literature review of racial/ethnic disparities in infertility care and treatment. Lower clinical pregnancy and live birth rates have been found collectively in Asian, Hispanic, and Black women in comparison to White women based on analyses of the Society for Assisted Reproductive Technology Clinic Outcome Reporting System data, with the trend of Black women having the poorest outcomes of all minority groups (11, 13–15). Determining the precise prevalence of infertility can be difficult. However, a study assessing racial differences in self-reported infertility found that Black women had a twofold increased odds of infertility compared with White women, after adjusting for socioeconomic status, pregnancy intent, and infertility risk factors (12). Furthermore, it has been shown that Black women are significantly less likely to seek care and use infertility treatment, even when insurance coverage is available (6).

Third-Party Reproduction and Race

Reproductive racial and socioeconomic disparities also permeate the subfield of third-party reproduction. Black women are generally underrepresented among patients using third-party ART, as shown by Shapiro et al. (10), through Society for Assisted Reproductive Technology data. Although Black women were more likely to use donor sperm, they were less likely to use donor oocytes or embryos and less likely to use gestational carriers despite a higher prevalence of fibroids. When Black women do seek use of donor oocytes and embryos, recent studies have found that they experience lower clinical pregnancy and live birth rates after embryo transfer, irrespective of using racially concordant donor oocytes and despite controlling for donor characteristics and cycle parameters (16, 17).

A barrier often faced by Black women who wish to use donor gametes is the sparsity of race-concordant gametes, from Black egg and sperm donors (18–20). In 2018, California Cryobank, one of the largest sperm banks in the US, carried only 17 Black sperm donors in its inventory (20). Similar shortages of egg donors were found in other developed nations, such as Great Britain, where in 2017 only 35 self-identified as Black and 1,608 as White (19). The suggested causes for this include lack of awareness, cultural/social stigma, religious taboo, and mistrust of the medical system within the Black community (18, 19). In November 2020, the American Society for Reproductive Medicine Diversity, Equity and Inclusion Task Force concluded that "the lack of people of color in key positions in our profession, high price of treatment, inaccessibility of medical care, differences in success rates, lack of accessible patient education, and implicit biases and discrimination by some offices pose immense burdens to infertile individuals of diverse backgrounds, in same sex relationships or who are without a partner" (21).

The case presented at the beginning of this article shines a light on the specific subset of minority women suffering from infertility who face a multitude of inherent barriers to successful pregnancy. Many essentially face no options, despite living in an age of momentous successes and advances in ART.

Ethically, this situation challenges the widely held concept of justice and provides an example of what has been called "stratified reproduction". Stratified reproduction describes a difference in valuation of the fertility of a certain group over another by those with social and political power (22). From the beginning of US history, the reproductive autonomy of Black and other minority women has been undervalued. The mechanisms at place that enforces stratified reproduction have been as stark as in the era of slavery during which enslaved Black women were valued based on their ability to breed more slaves, to the 1900s–1970s, when Black women were sterilized without consent as a form of eugenic population control endorsed by the US government (22). In the current era, stratified reproduction persists through basic socioeconomic differences that, for many, leads to unequal access to the medical interventions necessary to have true reproductive freedom. As per the American Society for Reproductive Medicine, "Reproduction is a fundamental interest and human right, and the access, treatment, and outcome disparities that are associated with infertility care and ART are a form of stratified reproduction that warrants correction" (23).

Call to Action

To actively dismantle this equity gap, we must target these barriers through awareness, advocacy, research, and education. The following is a list of action items that we encourage our readers to partake in as we collectively continue to advocate for justice in infertility care, with an emphasis on third-party reproduction:

1. Participate and support reproductive advocacy groups at the local, state, and federal levels to mandate oocyte cryopreservation, IVF, and third-party reproduction coverage universally.
2. Conduct behavioral and implementation studies, including focus group assessments, to further investigate the root causes for the disparities found within gamete donation, which specifically expound on the following:
   - What factors deter minorities from donating?
   - What can be done to encourage minorities to donate?
3. Petition for additional resources to support the described studies listed above, such as government-funded and privately funded grants.
4. Advocate for third-party agencies to put greater effort toward recruiting more minorities to donate through:
   - Equal compensation
   - Public education
   - Focused advertisements via social media and electronic applications that are developed to target a wider array of demographics
   - Extensive medical transparency, in regard to the medical process of donating, minimal risks involved, and comparative popularity in donating among other groups

- Recruit prominent social figures who have used such services to share their stories to demystify misunderstandings about the processes involved
- Consideration toward standardizing additional substantial incentives, such as a free oocyte cryopreservation cycle for personal future use
- Collaborate with fertility-focused medical societies, thereby presenting a joint mission of inclusivity

In conclusion, the field of ART has evolved at an exponential rate, yet unfortunately, it benefits some and not all. Therefore, it is imperative that when we advocate for full spectrum infertility care, that this encompasses everyone. Effectively narrowing the gap in third-party reproduction will inevitably require time, persistence, education, and patience. As we continue to further study and develop ART, we must not forget to consider the factors leading to racial and socioeconomic disparities in reproductive care access, utilization, and outcomes.

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