Time to pregnancy: as important for patients as underestimated by doctors

How many couples that have not yet become parents abandon in vitro fertilization (IVF) treatment owing to the psychological burden associated with treatment failure? Psychological stress is by far the most important factor in IVF treatment termination. Up to 50% of patients change doctors after their first IVF attempt. In the United States, up to 65.2% of patients with health insurance coverage that would be eligible to undergo another IVF treatment after a failed treatment do not seek further care (1). This discontinuation of treatment among insured patients is most commonly attributed to psychological burdens, including feeling too stressed to continue and the strain of infertility on the couple's relationship.

Even in countries where the government pays for three to six IVF cycles, about one-third of patients abandon treatment after at least one failed IVF cycle, highlighting the importance of the first IVF attempt (2). In contrast, in many developing nations, there is no IVF insurance or government coverage, so patients must pay for treatment out of their own pockets. As a result, many patients spend their lifetime financial savings for access to one IVF attempt, which most likely will result in failure. Furthermore, patients without IVF insurance coverage have threefold higher odds of treatment discontinuation compared with women with IVF insurance coverage (3). Therefore, although treatment costs are an important consideration at all times, there is a critical need to evaluate treatment effectiveness from the first cycle. Patients who choose to discontinue could, indeed, have a favorable prognosis and possibility to conceive, but psychological and financial pressures spoil their chance to have a biological child; patients may eventually regret this loss.

Several factors can converge in a "perfect storm" that prompts the discontinuation of IVF care after the first failed cycle. First, the clinical efficiency in terms of live birth rates (LBRs) remains low. Although this phenomenon has been known for decades, refinements and advances in reproductive treatments have not improved LBR at the first attempt per initiated cycle, which remains in the range of 25%–30% (4). Second, there is a lack of translational research bridging the gap between basic science and clinical application. Instead, this gap is occupied by whims that are immediately adopted by the medical community because they are easy to implement—such as scratching the uterus of a patient and pretending that it is a thoughtful treatment—or adding pills empirically, the last being an antidepressant. Finally, although robust meta-analyses are sometimes needed to summarize the current knowledge about a specific medical issue, such studies have become the Holy Grail in reproductive literature. Instead of critically revising the existing knowledge produced by randomized clinical trials (RCTs) and identifying biases, some meta-analyses are simply adding anything that might fit, like a "food processor," regardless of study quality and power. We have paid more attention to massaged poor-quality data through epidemiologic and statistical techniques than to creating high-quality data. For some topics, there are more meta-analyses than RCTs. In cooking terms, we need more excellent chefs than food critics to better understand the relationships among reproducibility, cumulative evidence, and the truth of clinical claims.

The metrics we use should be adapted to our main priority—that is, patient first—rather than preferred rules for clinicians or IVF centers. We have moved from the number of eggs retrieved or fertilization rates to cumulative live birth rate (CLBR) as a reliable way of reporting the success of an IVF program. The term cumulative means increasing in quantity by successive additions for patients repeatedly treated in one IVF center, incorporating all theoretical possibilities that are sitting in the freezer or in the cloud for all patients to conceive. From the patient perspective, the CLBR is informative after an unsuccessful cycle; but if the patient discontinues treatment, her CLBR will be 0. The main goal of an IVF treatment is for patients to bring home a healthy baby in the shortest period of time with the lowest number of embryo transfers performed. Patients are not interested in how many cycles it takes at a specific center for any patient to conceive; rather, they want to know their real chances to conceive a baby at the first attempt. This goal is relevant for specific interventions that will improve the success rate in terms of live birth at the first attempt—even if there will be no change in the CLBR, which is often used as an argument against adopting a technique that will benefit a patient in the first attempt. Worse yet, such interventions are reserved for implantation failure, when patients have attempted at least three unsuccessful cycles. However, because many patients will discontinue treatment after three failed attempts, they will never have an opportunity to implement a strategy that is only advocated by failure. Those proceeding with further treatments frequently ask why such a technique was not implemented earlier to enable them to avoid cycle failures, some of which ended in miscarriage and its associated medical risks and emotional distress.

These phenomena underscore that personalization in reproductive medicine must evolve considerably compared with other areas of medicine. The use of genetics and molecular diagnostics could lead to improvements in IVF treatment efficacy, and the potential benefits of such approaches should be discussed with patients in the first IVF attempt (5). We cannot defend the implementation of add-on treatments without an evidence base. Rather, we argue for a shift of mindset in the new decade: to use all available scientific evidence to support our patients in providing their best IVF treatment first, because sometimes the first treatment may be their only treatment, at least in our clinic. Furthermore, there is no economic rationale for either the patient or the doctor to undergo several failed cycles before offering the best possible care.

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