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SPECIAL ARTICLE

FIGO good practice recommendations on reduction of preterm birth in pregnancies conceived by assisted reproductive technologies

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Abstract

FIGO (the International Federation of Gynecology and Obstetrics) supports assisted reproductive technologies (ART) to achieve pregnancy and supports their availability in all nations. However, the increased frequency of preterm birth must be taken into account. Therefore, before in vitro fertilization (IVF) is started, other approaches, including expectant management, should be considered. Single embryo transfer is the best approach to ensure a live, healthy child. However, increased risks for preterm birth are also associated with a singleton IVF pregnancy and should be discussed and contrasted with spontaneous conception. Increased preterm birth and other adverse pregnancy outcomes in singleton IVF cycles warrant investigations to elucidate and mitigate. Minimizing embryo manipulation during cell culture is recommended. Increased risk of preterm birth and other pregnancy complications in ART could reflect the underlying reasons for infertility. This information should be discussed and further explored.

KEYWORDS
assisted reproductive technology, child outcome, preterm delivery, single embryo transfer

*The Members of the FIGO Working Group for Preterm Birth, 2018–2021, are listed at the end of the article.

1 | INTRODUCTION

Assisted reproductive technology (ART) is an essential component of infertility treatment. FIGO (the International Federation of Gynecology and Obstetrics) supports WHO in considering childbearing a human right that should be accessible in all nations. The social stigma of childlessness can lead to isolation and abandonment of women.[1] ART accounts for approximately 1%–2% of all pregnancies globally and as much as 7% in certain countries.[2] However, ART is also a significant risk factor for preterm birth, both in high-income and low–middle-income countries, and even in situations where single embryo transfer (SET) is applied.[3,4]

Recommendation: *FIGO supports ART to achieve pregnancy and supports its availability in all nations. However, the increased frequency of preterm birth and other pregnancy complications must be considered when starting ART.*

2 | TARGETED USE OF ASSISTED REPRODUCTIVE TECHNOLOGY

In vitro fertilization (IVF) should only be used if it is indispensable, i.e., if spontaneous conception or conception using less invasive methods have failed. This can be the case in infertile couples or individuals with diagnoses such as blocked tubes or severe male infertility that rule out spontaneous fertility chances. Otherwise, a prognosis for spontaneous conception could help.[5] In case of good prognosis, there might be benefit from expectant management or less invasive treatments with tubal flushing or intra-uterine insemination. Lifestyle interventions should also be considered for appropriate women. For example, in women with anovulation due to polycystic ovary syndrome, ovulation induction can be the first-line treatment. There are also other indications for IVF that are not covered in this document.

Recommendation: Before IVF is started, other approaches, including expectant management and other less invasive treatments, should be considered.

3 | SINGLE EMBRYO TRANSFER IN ASSISTED REPRODUCTIVE TECHNOLOGY

The US Centers for Disease Control and Prevention (CDC) states that double embryo transfer in ART results in a 27%–33% twin rate, whereas SET results in a 1% twin rate.[5,6] In addition, transferring multiple embryos is unequivocally correlated with preterm birth.[4,6] This strategy has long been advocated but has not been pursued rigorously. Given that ART is increasingly performed worldwide, increased rates of twins will continue unless SET is widely utilized. We realize the global differences, but there should never be a standard procedure to transfer multiple embryos.

Recommendation: *In treatment with IVF, single embryo transfer is the best approach to prevent multiple pregnancies and subsequent preterm birth, thus maximizing the chance of having a healthy live child.*

4 | PREGNANCY COMPLICATIONS IN ART

Less appreciated than in multiple gestation pregnancies is that singleton IVF pregnancies are also associated with increased preterm birth (two-fold), stillbirths, and intrauterine growth restriction. In addition, neonatal Intensive Care Unit (NICU) admissions are also increased.[7]

Meta-analyses of singleton IVF pregnancies have shown up to 10.9% preterm birth rates (<37 weeks of gestation) versus 6.4% in a comparison group delivered at full term.[8] Thus, singleton IVF pregnancy remains a risk factor for early preterm birth even after adjustment for other risk factors such as maternal age, smoking, or prior surgical procedures for cervical intraepithelial neoplasia or infertility.[8,9] Similarly, infertility or subfertility without ART is associated with increased adverse pregnancy outcomes compared with spontaneous pregnancies.[1] Association of ART with preterm birth is also evident from conception with intrauterine insemination or ovulation induction, as singleton pregnancies resuting from these treatments do not have increased preterm birth rates.[3]

Recommendation: Increased risks for preterm birth are associated with singleton IVF. This information should be discussed and contrasted with spontaneous conception.

The increased risk for preterm birth in singleton IVF pregnancies may reflect embryo manipulation inherent in successful ART. Embryo culture, freezing/thawing procedures and endometrial transfer itself may impair implantation or the ability to maintain a pregnancy and influence the neonatal outcome.[10] Significant differences in preterm birth rates and other adverse pregnancy outcomes are observed when comparing different culture media or fresh and frozen transfer, perhaps leading to abnormal placentation.[9,11] Abnormalities of placental function as an explanation are suggested by increased maternal β-hCG and decreased pregnancy-associated plasma during early pregnancy.[12,13]

Recommendation: *Increased preterm birth and other adverse pregnancy outcomes in singleton IVF cycles warrant investigations to elucidate and mitigate. Therefore, minimizing embryo manipulation during cell culture is recommended.*

An alternative explanation for increased preterm birth and other adverse outcomes in singleton IVF cycles is that these outcomes could reflect the underlying reason why ART infertility was required to achieve a pregnancy. By analogy, birth defects are increased 30% (odds ratio 1.3) in offspring conceived using IVF or intra-cytoplasmic sperm injection (ICSI).[14,15] Moreover, birth defects are increased by 20% in subfertile women whose time to conceive is delayed (>1 year) but who never required IVF or ICSI.[16]

Recommendation: Increased risks for preterm birth and other pregnancy complications in ART could reflect the underlying reasons for infertility. This information should be discussed.

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CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

All authors and the FIGO Working Group for Preterm Birth drafted the concept of the paper. KM wrote the first version of the manuscript. BWM, BJ, and WAG revised various versions of the manuscript. All authors and working group members commented on the manuscript and approved the final version of the manuscript.

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