



## **IVF/ICSI treatment and the risk of iatrogenic preterm birth in singleton pregnancies: a meta-analysis of cohort studies**

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### **Objective**

Preterm birth (PTB) is more frequent among in-vitro fertilization (IVF) as compared to natural conception and recent research in this group describes an increase of its spontaneous aetiology. This study quantifies the risk of iatrogenic preterm birth (IPTB) in singleton pregnancies resulting from IVF/ICSI as compared to spontaneous conception.

### **Methods**

Web-based databases search (PubMed/Medline, Scopus, Web of Science) up to January 2018 detected papers comparing the risk of IPTB in IVF/ICSI and naturally conceived singleton pregnancies. Screening of original studies assessed for eligibility identified 9 papers meeting the inclusion criteria: conception with IVF/ICSI, PTB defined as delivery below 37 weeks, cohort design with clear distinction of spontaneous and indicated PTB. Primary outcome was IPTB<37 weeks. Counting of IPTB was done both directly extracting data when available and calculated indirectly (IPTB= total preterm birth – spontaneous preterm birth). Relevant secondary outcomes were also analysed. A meta-analysis calculated the risk of IPTB in IVF/ICSI pregnancies.

### **Results**

Pooled crude analysis of the primary outcome with indirect calculation showed a total sample size of 9, 595 births and a significant increase in IPTB<37 weeks (IVF/ICSI: 179/4321; [4. 14%] and spontaneous: 98/5274; [1. 85%]; OR=2. 44; 95% CI: 1. 44–4. 14; I<sup>2</sup>=66%). Pooled crude analysis of the primary outcome with direct counting showed a total sample size of 6, 506 births and a significant increase in IPTB<37 weeks (IVF/ICSI: 143/3160; [4. 52%] and spontaneous: 76/3346; [2. 27%]; OR=2. 51; 95% CI: 1. 32–4. 78; I<sup>2</sup>=72%). Sensitivity analysis of studies with higher quality (NOS>7) maintained the significance (OR 2. 32, 95% CI: 1. 19-4. 51; I<sup>2</sup>=75%). Pooled analysis of IPTB due to fetal growth restriction and abnormal cardiotocography failed to show statistical significance, whereas IPTB due to abruptio placentae showed a total sample size of 561 and a significant increase (IVF/ICSI: 7/225; [3. 11%] and spontaneous: 2/327; [0. 61%]; OR=5. 41; 95% CI: 1. 26-23. 25; I<sup>2</sup>: 0%).

### **Conclusion**

The risk of IPTB<37 weeks in singleton pregnancies achieved with IVF/ICSI is significantly greater than that from natural conception and abruptio placentae is an important contributor to this outcome.