

# Risk of stillbirth 4 times higher after IVF/ICSI compared to spontaneous pregnancies

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Women who become pregnant with a single foetus after in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) have an increased risk of a stillbirth, according to new research out today.

The study of over 20,000 singleton pregnancies, published in Europe's leading reproductive medicine journal [Human Reproduction](#), found a four-fold increased risk of stillbirths for women who had IVF/ICSI compared with women who conceived spontaneously or after fertility treatment that did not involve IVF or ICSI.

However, the authors of the Danish study say that these results should be interpreted carefully. Dr Kirsten Wisborg, who led the study, said: "It is important to remember that the risk of [stillbirth](#) is still very low among women pregnant after IVF/ICSI. At this stage we do not know whether the increased risk in women pregnant after IVF/ICSI is due to the fertility treatment or to unknown factors pertaining to couples who undergo IVF/ICSI. This needs further investigation."

Dr Wisborg, who is a consultant in the neonatal and intensive care unit at Aarhus University Hospital (Aarhus, Denmark), and colleagues analysed data that had been collected prospectively from unselected, pregnant women taking part in the Aarhus Birth Cohort. The study included information on women booked for delivery between August 1989 and October 2006. Information on obstetric history, including waiting times to pregnancy and fertility treatments, age, smoking habits during pregnancy, alcohol and coffee intake during pregnancy, marital status, education and any psychological problems was collected in two questionnaires completed before the first routine antenatal visit at 16 weeks gestation.

Out of a total of 20,166 singleton, first-time pregnancies, 16,525 (82%) were conceived spontaneously after less than 12 months, 2,020

(10%) after more than a year of trying (classified as sub-fertile), 879 (4%) conceived after non-IVF fertility treatment and 742 (4%) conceived after IVF/ICSI. There was a total of 86 stillbirths, giving an overall risk of stillbirth of 4.3 per thousand pregnancies.

The risk of stillbirth in women who conceived after IVF/ICSI was 16.2 per thousand; in women who conceived after non-IVF fertility treatment it was 2.3 per thousand; in fertile and sub-fertile women, the risk was 3.7 per thousand and 5.4 per thousand respectively.

Dr Wisborg said: "After adjusting for maternal age, body mass index, education, smoking habits and alcohol and coffee intake during pregnancy we found a significant, four-fold increased risk of stillbirth in women who conceived after IVF/ICSI compared with fertile women. The risk of stillbirth in sub-fertile women and women who conceived after non-IVF fertility treatment was not statistically significantly different from the risk in fertile women.

"Until now, there has been speculation that the increased risk of adverse outcomes, such as stillbirths, in assisted reproduction might be due to factors related to the underlying infertility of the couples. However, we found the risk was similar between sub-fertile couples, women who had conceived after non-IVF fertility treatment and fertile couples. This may indicate that the increased risk of stillbirth is not explained by infertility and may be due to other, as yet unexplained factors, such as the technology involved in IVF/ICSI or some physiological difference in the couples that require IVF/ICSI."

She added: "IVF and ICSI patients represent a group resistant to low-technology infertility treatment and have a longer infertility period; they may, accordingly, be selected by unknown factors associated with an increased risk of stillbirth."

Dr Wisborg and her colleagues are continuing to collect data in order to find answers to some of the questions on the association between stillbirths and fertility treatment. "One of the very important things to study in detail is the causes of stillbirth. We know from our data that gestational age at delivery was four weeks lower in stillborn infants of IVF pregnant women compared to stillborn infants of women who conceived spontaneously. However, despite the size of our study we did not have enough data to study this question in more detail," she said.

She concluded: "Hopefully, the results from our study emphasize the need for continuous follow-up of the outcome of fertility treatments, so that the information given to infertile couples seeking treatment can be differentiated to their individual circumstances."

Between 1989 and 2006 there were several changes and improvements made in IVF techniques. However, the researchers say this is unlikely to have influenced their results as analyzing data stratified according to an early and a late study period made no changes to their conclusions. In addition, to preterm births, another potential confounding factor could be the so-called "vanishing twin" phenomenon. Around 10% of singleton pregnancies are thought to originate from twin gestations because of the transfer of two or more embryos. Compared with singleton conceptions, these pregnancies carry an increased risk of preterm delivery and low birth weight. However, the authors believe this is unlikely to be the sole reason for their results because the risk of stillbirth in non-IVF pregnancies was similar to that in fertile women.

**More information:** IVF and stillbirth: a prospective follow-up study. *Human Reproduction* journal. doi:10/1093/humrep/deq023

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