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Is IVF making more male embryos and does maternal AMH play a role in this?

Karissa Hammer, MD [1] ; Panagiotis Cherouveim, MD [1] ; Kaitlyn James, MD, PhD [1] ; Irene Souter, MD [1] ; Charles Bormann, PhD [1] ; Mary Morris, MD, PhD [1] ; David Pepin, PhD [1]

1. Massachusetts General Hospital/Harvard Medical School, Department of Obstetrics and Gynecology

Abstract

STUDY QUESTION: Does a high maternal AMH environment during oocyte maturation affects in vitro preimplantation embryo development resulting in a sex skew toward male live births

STUDY ANSWER: Increasing AMH levels correlate with an increased trend for male births after in vitro conception (IVF) but not with in vivo (intrauterine insemination, IUI) conception.

WHAT IS ALREADY KNOWN: A sex skew toward male neonates after IVF has been described, but it is unclear why this skew exists [1] . This phenomenon may be related to speed at which a male embryo develops to the blastocyst stage leading to an increase in their selection for transfer. We propose that maternal AMH also plays a role in early embryonic development. AMH is known for its role in sexual differentiation and as a marker for ovarian reserve. AMH receptor has been heavily identified in male placentae and fetal membranes and likely impacts early embryonic development [2] .

STUD DESIGN, SIZE, DURATION: Retrospective data analysis of live births from IUI and IVF cycles between January 2015 to December 2021 at an academic institution in the United States. Primary outcome was the rate of male versus female live birth analyzed by maternal AMH. Exclusion criteria included use of donor oocytes, cycle cancellation, missing AMH values, fetal loss and PCOS diagnosis.

PARTICIPANTS/MATERIALS, SETTING METHODS: The IVF and IUI dataset included women ages 27 - 44 with an AMH level drawn within one year of treatment. Results were analyzed by AMH level within quartiles and as a continuous variable.

MAIN RESULTS AND THE ROLE OF CHANCE: The IUI population consisted of 1089 live births, after exclusions 325 live births were analyzed. AMH levels were similar between males and females born after IUI (median [IQR]: female 3.0 [1.6, 4.5] and male 2.6 [1.4, 4.3], p 0.29). AMH analyzed continuously had an OR 0.99 (95%CI 0.97, 1.01) and compared to those below the 75%ile those with maternal AMH above the 75th percentile (AMH 5ng/mL) had an OR 0.92 (95%CI 0.79, 1.07) for male live birth. The odds rations were adjusted for maternal age, BMI, and sperm type (fresh vs frozen). The IUI population did not show a correlation with AMH and male neonates at birth.

The IVF population had 698 live births, after exclusions 406 were analyzed. AMH levels did differ significantly between male and female live births (median [IQR]: female 2.7[1.55, 4.4] and male 3.5 [1.6, 5.8], p=0.012). Odds for male live birth increased with increasing levels of AMH, both when analyzed as a continuous variable with an adjusted OR 1.12 (95%CI 1.04, 1.13, p<0.05) and when analyzed as quartile increment, [AMH above the 75%ile (AMH 5ng/mL) had an adjusted OR

2.06 (95%CI 1.30,3.25, p<0.05)]. Adjustments were made for maternal age, BMI, number of fertilized oocytes and cycle type (fresh vs frozen).

LIMITATIONS, REASONS FOR CAUTION: This is a retrospective review of ART data from a single center, more work is needed to elucidate how AMH exposure of the oocyte may affect subsequent and development of male vs female embryos.

WIDER IMPLICATIONS OF THE FINDINGS: AMH levels are correlated with increased odds for male live birth after IVF, but the mechanism for why this occurs is unclear. Further investigation is warranted to understand sex differences in embryo development so as not to artificially skew the sex ratio when selecting embryos for transfer.

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