fortune Journals

Research Article

OBSTETRICS AND GYNECOLOGY RESEARCH

ISSN: 2637-4560

Outcome Following Oocyte Retrieval in Women with Marked Diminished Oocyte Reserve Where the Only Oocyte Obtained Was in A Metaphase I Stage

Jerome H Check MD, Ph.D.[1,2*], Donna Summers MS[2], Danya Horwath MS[2], Madison Neulander BS[2], Brooke A Neumann DO[3]

Abstract

Women with marked diminished oocyte reserve (DOR) may still require in vitro fertilization embryo transfer (IVF-ET) because of severe male subfertility or damaged fallopian tubes. Live deliveries have been reported even with only one oocyte retrieved, especially with a mild ovarian stimulation technique known as the FSH receptor up-regulation technique. Though live deliveries have been reported using rescued metaphase (M) I oocytes cultured to the MII stage, live delivered pregnancy rates (LDPRs) are markedly reduced. The purpose of this study was to determine if a live delivery is possible where the only oocyte retrieved was a MI oocyte who already has a much reduced chance of conception even if a MII oocyte had been obtained. A 25- year retrospective study identified 42 women aged ≤ 39.9 and 40 women ≥ age 40 who had only a single MI egg retrieved. In the younger group, 14 women proceeded to ET 4 days after egg retrieval and 1 had a live delivery. For women ≥40, 15 women proceeded to ET but there were no live deliveries. Since a precedent has been set that a live delivery is possible, despite marked DOR and one MI egg retrieved, it seems reasonable to advise extended culture with the hope of transferring a viable embryo.

Keywords: Diminished oocyte reserve; Rescued oocyte; Metaphase I; Fresh embryo transfer

Introduction

In women with normal oocyte reserve undergoing in vitro fertilization embryo transfer (IVF-ET) with normal oocyte reserve (NOR) it is estimated that one could expect about 80-85% of the oocytes retrieved to be fully mature, i.e., they are in the metaphase II (MII) stage with 15-20% immature oocytes (germinal vesicle stage or MI stage) [1]. Culturing metaphase I oocytes or even germinal vesicle stage embryos another day, followed by fertilization by intracytoplasmic sperm injection (ICSI) (because the zona pellucida has been stripped) results in a much lower percentage of euploid embryos compared to those inseminated on the day of oocyte retrieval [2-4]. Conti and Franciosi, suggested that the low fertility potential of these rescued immature oocytes is related to lack of coordination of the normal events leading to euploidy of the zygote including coordination of fertilization events, reprogramming of the parental genomes, DNA replication, and embryonic genomic activation [5]. Indeed, most studies suspect that in vitro mature rescued MI oocyte lead to a much higher chance of an aneuploid embryo [6-9].

There have been live deliveries reported following culturing of MI to MII oocyte with subsequent embryo transfer dating back to the late 1990s [10,11].

Affiliation:

[1]Cooper Medical School of Rowan University, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ

[2]Cooper Institute for Reproductive Hormonal Disorders, P.C. Mt. Laurel, NJ

[3]Inspira Health Network Vineland, NJ

***Corresponding author:**
Jerome H Check MD, Ph.D. Outcome Following Oocyte Retrieval in Women with Marked Diminished Oocyte Reserve Where the Only Oocyte Obtained Was in A Metaphase I Stage.

Citation: Jerome H Check, Donna Summers, Danya Horwath, Madison Neulander, Brooke A Neumann DO. Outcome Following Oocyte Retrieval in Women with Marked Diminished Oocyte Reserve Where the Only Oocyte Obtained Was in A Metaphase I Stage. Obstetrics and Gynecology Research. 8 (2025): 42-45.

Received: November 21, 2024
Accepted: November 28, 2024
Published: February 15, 2025

Jerome H Check MD, et al., Obstet Gynecol Res 2025
DOI:10.26502/ogr0177

These early studies simply transferred the embryos cultured for two days on the 3rd day after oocyte retrieval in contrast to M-II oocytes fertilized on the day of retrieval that would be allowed to develop for 3 days prior to embryo transfer. Though the appearance of morphologically normal appearing embryos reported in some studies was reasonable, and sometimes comparable to embryos derived from fertilization of retrieved MII oocytes, the live delivered pregnancy rates (LDPRs) were poor. For example, in the aforementioned study by Reichman et al, though they demonstrated similar fertilization rates of MI oocyte vs MII oocytes, embryo quality was only half as good. They had no live deliveries out of 17 embryos obtained by extended culture and delayed fertilization [4].

As mentioned, rescued oocytes seem to have lower fertilization rates [2-4, 12,13]. However, some claim that the embryo quality as determined by embryo morphology may be similar [12]. Nevertheless, these rescued oocytes seem to have defective cytoplasmic maturation, increased meiotic aberrations, and nuclear degeneration (14). Normal morphologic embryos lead to similar blastocyst formation, but yet higher rates of aneuploidy [15]. Furthermore, there is a difference in the morphokinetic characteristics of embryos derived from in-vitro matured vs in vivo matured oocytes after ovarian stimulation [16].

There may be one other explanation for lower pregnancy rates following the fresh transfer of embryos derived from rescued vs embryos from fertilization of MII oocytes and that is the possible adverse consequence of asynchrony between the stage of embryo development vs endometrial development, i.e., placing either day 3 embryos or blastocysts in the uterine cavity that is one day earlier than if the egg was fertilized on the day of retrieval. Thus, Ming et al found a higher pregnancy rate if instead of transferring fresh to a uterus with an asynchronous endometrium, to freeze the embryos derived from the fertilization of a rescued oocyte and delay transfer of the frozen thawed embryos in a subsequent cycle where proper synchronization could be achieved [17]. Aizer et al found that the LDPR following fresh embryo transfer derived from rescued oocytes was 1.6% vs 8.3% with frozen-thawed embryos derived from rescued oocyte embryos transferred to the uterus with a synchronous stage of development as the frozen-thawed embryo [18]. A live fetus in the 1st trimester was reported in a poor responder using a rescued oocyte. However, the patient was an unexpected non responder with no evidence of DOR before ovarian hyperstimulation [19].

Most infertility centers will cancel an IVF-ET cycle if they expect to retrieve only 1 or 2 oocytes. The majority of infertility centers will advocate the use of donor oocytes if there is marked diminished oocyte reserve (DOR). Nevertheless, at our institution we have had considerable experience in helping women with marked DOR to become pregnant with their own oocytes. For over 40 years, since we published a novel technique on restoring down-regulated FSH receptors in women in apparent premature ovarian failure (POF) that not only results in the induction of ovulation but also achieved live deliveries [20-22].

We encourage women with DOR to conceive without IVF-ET because without multiple oocytes to create more embryos it does not seem prudent to encounter the increased expense and invasiveness of IVF-ET. However, when there is a need for IVF, e.g. damaged fallopian tubes or a severe sperm defect, it is reasonable to consider IVF-ET even if there is a likelihood of only one egg being retrieved, or even with the combination of DOR and advanced age [23-25].

The question arises as to whether it is worthwhile to culture an MI oocyte to the MII stage in women with such severe DOR that they can only develop 1 dominant follicle, or in women that appear to be in overt menopause where development of a dominant follicle is attained by techniques aimed to up-regulate down-regulated FSH receptors [26, 27].

Material and Methods

A retrospective review was performed over a 25-year time period to identify women having such severe DOR that there was only one oocyte retrieved. The number of patients with a single metaphase II oocyte vs metaphase I was determined. Very immature oocytes, i.e., germinal vesicle stage, were not included. Following fertilization of the MI to MII oocytes. The embryos continued culture and were transferred fresh 4 days from the oocyte retrieval.

The oocyte stimulated protocol was a specific type of mild stimulation protocol known as an FSH receptor upregulation technique [27]. Details of the variations in this protocol according to the patients' serum hormonal levels (LH, FSH, estradiol (E2) and progesterone (P)) have been provided [27] This protocol may vary from patient to patient or cycle to cycle in the same patient [27]. There is evidence that this stimulation protocol maximizes the chance of a successful pregnancy based on evidence that raising the serum FSH too high can down-regulate a key FSH dependent cytokine or enzyme needed for the embryo to implant and the fetus to survive [28, 29].

Results

There were 42 women aged ≤39.9 who had a single MI oocyte cultured to MII. Fertilization occurred in 24 of 42 (53.9%) and cleavage to day 3 occurred in 18 of the 24 women (75%). Fourteen women had a fresh ET and 4 cryopreserved the embryo. None of the 4 women with cryopreserved embryos had a subsequent single embryo transfer so they were not included in the data. Two of the 14 women (14.3%) having a fresh ET conceived and had ultrasound evidence of pregnancy (clinical pregnancy) and 1 had a successful full-term delivery of a healthy child (7.1%)

Citation: Jerome H Check, Donna Summers, Danya Horwath, Madison Neulander, Brooke A Neumann DO. Outcome Following Oocyte Retrieval in Women with Marked Diminished Oocyte Reserve Where the Only Oocyte Obtained Was in A Metaphase I Stage. Obstetrics and Gynecology Research. 8 (2025): 42-45.

Jerome H Check MD, et al., Obstet Gynecol Res 2025
DOI:10.26502/ogr0177

There were 40 women > 40 where the sole oocyte retrieved was in the metaphase I stage. Fertilization occurred in 23 of 42 (54.8%) leading to 15 of 23 (65.2%) cleaved embryos to transfer; however, there were no pregnancies.

Discussion

In using the FSH receptor up regulation technique to mature oocytes for oocyte retrieval, live delivered pregnancy rates per (LDPRs) per transfer of a single embryo derived from an MII oocyte for women < age 39 is between 20-25% [25, 27-33]. This study shows that despite the appearance of normal morphologic embryos that were obtained from rescued oocytes, these embryos are much less likely to produce a live delivered baby. Nevertheless, a live delivery is possible (at least in women aged <39.9 and thus if they have already proceeded to oocyte retrieval) there does not seem to be any downside to culturing the rescued oocyte to the MII stage and do an embryo transfer. Whether higher pregnancy rates would be achieved by deferring fresh transfer and cryopreserving the embryo to allow a more synchronized transfer with luteal P effect on the endometrium in a subsequent cycle is at least possible [17, 18].

Women with extremely low oocyte reserve have a very reduced chance of conceiving a live baby with or without IVF-ET. Thus, IVF should be restricted to couples that require the procedure for damaged tubes or very poor sperm quality. This is the first case demonstrating that a live delivery is possible even when the only oocyte retrieved is MI oocyte and the woman has severe DOR.

Conclusion

In women with such severe DOR that there is only 1 oocyte to retrieve, one must consider that this group is much different than the previous publications of outcomes of rescued MI oocytes. Even those reporting outcome in poor responders, the finding of the poor response and the presence of only immature oocytes was unexpected, i.e., not predicted by serum AMH level or day 3 FSH. Furthermore, in the past fresh embryos were transferred 3 days after oocyte retrieval. We believe that this is the first evaluation of transfer of day 3 embryos, 4 days after oocyte retrieval, thus, allowing assisted embryo hatching.

References

1. Shin SB, Cho JW, Lee SH, et al. Fertilization and pregnancy potential of immature oocytes from stimulated intracytoplasmic sperm injection cycles. Clin Exp Reprod Med 40 (2013): 7-11.
2. Strassburger D, Friedler S, Raziel A, et al. The outcome of ICSI of immature MI oocytes and rescued in vitro matured MII oocytes. Hum Reprod 19 (2004): 1587-1590.
3. Shu Y, Gebhardt J, Watt J, et al. Fertilization, embryo development, and clinical outcome of immature oocytes from stimulated intracytoplasmic sperm injection cycles. Fertil Steril 87 (2007): 1022-1027.
4. Reichman DE, Politch J, Ginsburg ES, et al. Extended in vitro maturation of immature oocytes from stimulated cycles: an analysis of fertilization potential, embryo development, and reproductive outcomes. J Assisted Reprod Genet 27 (2010): 347-356.
5. Conti M, Franciosi F. Acquistion of oocyte competence to develop as an embryo: integrated nuclear and cytoplasmic events. Hum Reprod Update 24 (2018): 245-266.
6. Nogueira D, Staessen C, Van de Velde H, et al. Nuclear status and cytogenetics of embryos derived from in vitro-matured oocytes. Fertil Steril 74 (2000): 295-298.
7. Emery BR, Wilcox AL, Aoki VW, et al. In vitro oocyte maturation and subsequent delayed fertilization is associated with increased embryo aneuploidy. Fertil Steril. 84 (2005):1027-1029.
8. Moon JH, Zhao Q, Zhang J, et al. The developmental competence of human metaphase I oocytes with delayed maturation in vitro. Fertil Steril 119 (2023): 690-696.
9. Escrich L, Galiana Y, Grau N, et al. Do immature and mature sibling oocytes recovered from stimulated cycles have the same reproductive potential? Reprod Biomed Online 37 (2018): 667-676.
10. Edirisinghe WR, Junk SM, Matson PL, et al. Birth from cryopreserved embryos following in-vitro maturation of oocytes and intracytoplasmic sperm injection. Hum Reprod 12 (1997): 1056-1058.
11. Tucker MJ, Wright G, Morton PC, et al. Birth after cryopreservation of immature oocytes with subsequent in vitro maturation. Fertil Steril 70 (1998): 578-579.
12. De Vos A, Van de Velde H, Joris H, et al. In vitro matured metaphase-I oocytes have a lower fertilization rate but similar embryo quality as mature metaphase-II oocytes after intracytoplasmic sperm injection. Hum Reprod 14 (1999): 1859-1863.
13. Alvarez C, Garcia-Garrido C, Taronger R, et al. In vitro maturation, fertilization, embryo development & clinical outcome of human metaphase-I oocytes retrieved from stimulated intracytoplasmic sperm injection cycles. Indian J Med Res 137 (2013): 331-338.
14. Rackowsky C, Kaufman ML. Nuclear degeneration and meiotic aberrations observed in human oocytes matured in vitro: analysis by light microscopy. Fertil Steril 58 (1992): 750-755.
15. Sachdev NM, Grifo J, Licciardi F. Delayed intracytoplasmic sperm injection (ICSI) with trophectoderm biopsy and preimplantation genetic screening (PGS) show increased aneuploidy rates but can lead to live births with single

Jerome H Check MD, et al., Obstet Gynecol Res 2025
DOI:10.26502/ogr0177

thawed euploid embryo transfer (STEET). J Assist Reprod Genet 33 (2016): 1501-1505.

16. Margalit T, Ben-Haroush A, Garor R, et al. Morphokinetic characteristics of embryos derived from in-vitro-matured oocytes and their in-vivo-matured siblings after ovarian stimulation. Reprod Biomed online 38 (2019): 7-11.

17. Ming L, Liu P, Qiao J, et al. Synchronization between embryo development and endometrium is a contributing factor for rescue ICSI outcome. Reprod Biomed online 24 (2012): 527-531.

18. Aizer A, Noach-Hirsh M, Gitman H, et al. Embryos derived from delayed mature oocyte should be cryopreserved and are favourable to transfer in a following endometrium synchronize frozen-thawed cycle. Zygote 30 (2022): 689-694.

19. Yalcinkaya E, Caliskan E, Budak O. In vitro maturation may prevent the cancellation of in vitro fertilization cycles in poor responder patients: a case report. J Turk Ger Gynecol Assoc 14 (2013): 235-237.

20. Check JH, Chase J. Ovulation induction in hypergonadotropic amenorrhea with estrogen and human menopausal gonadotropin therapy. Fertil Steril 42 (1984): 919-922.

21. Check JH, Nowroozi K, Chase JS, et al. Ovulation induction and pregnancies in 100 consecutive women with hypergonadotropic amenorrhea. Fertil Steril 53 (1990): 811-816.

22. Check ML, Check JH, Choe JK, et al. Successful pregnancy in a 42-year-old woman with imminent ovarian failure following ovulation induction with ethinyl estradiol without gonadotropins and in vitro fertilization. Clin Exp Obstet Gynecol 29 (2002):11-14.

23. Check JH, Choe JK, Cohen R: Successful pregnancy following a single fresh embryo transfer in a 45-year-old woman whose early follicular phase serum follicle stimulating hormone was 29 mIU/mL. Clin Exp Obstet Gynecol 38 (2011): 335-337.

24. Check JH, Chern R, Amui J. Successful pregnancy following in vitro fertilization embryo transfer in a 46-year-old woman with diminished oocyte reserve as evidenced by a high day 3 serum estradiol. Clin Exp Obstet Gynecol 38 (2011): 209-210.

25. Check JH, Summers-Chase D, Yuan W, et al. Effect of embryo quality on pregnancy outcome following single embryo transfer in women with a diminished egg reserve. Fertil Steril 87 (2007): 749-56.

26. Check JH. Physicians should be more open-minded about performing in vitro fertilization-embryo transfer in women with diminished oocyte reserve and consider the couple's wishes and desires. Clin Exp Obstet Gynecol 39 (2012): 5-10.

27. Check JH, Wilson C, DiAntonio G, et al. In vitro fertilization (IVF) outcome in women in overt menopause attempting to induce follicular maturation by follicle stimulating hormone (FSH) receptor down-regulation. Clin Exp Obst Gynecol 43 (2016): 181-183.

28. Check JH. Optimizing IVF outcomes for women with diminished oocyte reserve. Expert Rev Obstet Gynecol 8 (2013): 401-415.

29. Check JH. A follicle stimulating hormone (FSH) receptor up-regulation technique as a method for follicular recruitment for in vitro fertilization-embryo transfer in women with diminished oocyte review. Ed. Leon V. Berhardt; In: Advances in Medicine and Biology, Nova Science Publishers, Inc., Hauppauge, NY 195 (2022): 119-137.

30. Check JH, Whetstone A, Choe JK, Cohen R. The effect of oocyte reserve on pregnancy rates per oocyte harvest in women aged 36-39. Clin Exp Obstet Gynecol 42 (2015): 573-575.

31. Check JH, Wilson C. The younger the patients the less adverse effect of diminished oocyte reserve on outcome following in vitro fertilization-embryo transfer as long as the proper ovarian stimulation protocol is used. J Reprod Contracep 24 (2013): 221-227.

32. Check JH, Neumann B, Check DL, Sobel M. A study to determine the reason for lower pregnancy rates in younger woman with diminished oocyte reserve –less chance of implementing vs feral demise. IgMin Res (2024): 364-366.

33. Yalcinkaya E, Caliskan E, Budak O. In vitro maturation may prevent the cancellation of in vitro fertilization cycles in poor responder patients: a case report. J Turk Ger Gynceol Assoc 14 (2013): 235-237.

Citation: Jerome H Check, Donna Summers, Danya Horwath, Madison Neulander, Brooke A Neumann DO. Outcome Following Oocyte Retrieval in Women with Marked Diminished Oocyte Reserve Where the Only Oocyte Obtained Was in A Metaphase I Stage. Obstetrics and Gynecology Research. 8 (2025): 42-45.