

# Quintuplet Pregnancy Following Transfer of Three Embryos. A Case Report.

Aya Naim Abusheikha (✉ [abusheikhaaya@gmail.com](mailto:abusheikhaaya@gmail.com))

UJ: The University of Jordan <https://orcid.org/0000-0002-3752-775X>

Naim A. Abusheikha

Al-Israa Hospital

Aseil E. Khatib

The University of Jordan

---

## Case report

**Keywords:** Multiple gestation, monozygotic, cleaved embryos, quintuplet, case report

**Posted Date:** January 8th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-138791/v1>

**License:** © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

**Background:** This is a rare case of a quintuplet pregnancy of two sets of monozygotic twins (MZT) co-existing with a singleton pregnancy resulting from transfer of three cleaved embryos. This has not been reported previously in humans, and should be kept in mind when replacing multiple embryos using in vitro fertilization.

**Case Presentation:** A 27 year old female had a successful twin livebirth after fetal reduction of unexpected quintuplet pregnancy following transfer of three embryos To ameliorate the adverse implications of multiple gestation, fetal reduction to twins by intracardiac puncture and aspiration was carried out at 11 weeks' gestation. The patient has now delivered two healthy babies (a boy and a girl) at 35 weeks and 6 days by a lower segment caesarean section.

**Conclusion:** Clinicians should keep in mind that patients undergoing assisted conception may develop monozygotic twinning of the embryos, which may negatively impact the pregnancy and raise an ethical and psychological dilemma for the patient.

## Background

The first monozygotic pregnancy resulting from IVF treatment was reported by Yovich et al. [1]. Patients at risk of monozygotic twinning are young patients, [2] those who had ovulation induction, [3] and those who had embryos with artificial breach of the zona pellucida, as in intra cytoplasmic sperm injection (ICSI) [4] and assisted hatching. [5] However, in view of the rarity of this phenomenon, these factors are not frequently taken in consideration when clinicians and patients decide on the number of embryos to be replaced.

Herein, we report a case of a successful twin livebirth after fetal reduction of unexpected quintuplet pregnancy following transfer of three embryos. A literature review of all monochorionic quadruplet pregnancies showed that there have been a few cases found, including one by Saravelos et al; who reported a monozygotic quadruplet pregnancy following single embryo transfer. [6] However, the distinguishing characteristic of our case is that it is the first quintuplet pregnancy in which monozygotic twinning in 2 embryos occurred simultaneously (co-existing with a singleton); a phenomenon which has not been reported previously in humans, only found in-vitro in mouse embryos. [7]

## Case Presentation

This patient was 27 years old with a one and half year history of primary subfertility secondary to polycystic ovarian syndrome along with a mild male factor infertility. She had previously made four unsuccessful attempts at ovulation induction. For her IVF cycle, a gonadotrophin hormone releasing hormone analogue together with a highly purified follicle stimulating hormone were used in a long protocol. [8] On the 11th day of stimulation 10,000 IU of urinary hCG was given for final oocyte maturation. Ultrasound-guided transvaginal egg recovery was performed 36 hours later. Ten oocytes were

retrieved, of which 7 were mature. Intracytoplasmic sperm injection (ICSI) was used for egg fertilization and 5 were successfully fertilized. Although we fully explained to the couple how the transfer of two good quality embryos gives almost the same success rates obtained with the transfer of three embryos, they insisted on placing 3 embryos as they perceived it as the best for achieving their goal. 3 (Grade 1; 6–8 cells) embryos were transferred easily to the uterine cavity and the remaining 2 embryos were cryopreserved for future use. The luteal phase was supported by Cyclogest vaginal pessaries at a dose of 400 mg twice daily (L.D. Collin, Barnstaple, UK).

The patient became pregnant as confirmed by a hCG level of 2610 IU/L on day 15 post-transfer. Routine two-dimensional (2D) transvaginal ultrasound on day 30 post-embryo transfer showed 3 gestational sacs with 5 viable fetuses; one of a singleton pregnancy and two of monochorionic monoamniotic twins. At 11 weeks' visit they were offered fetal reduction. Following a detailed consultation the couple accepted to have fetal reduction to twin pregnancy. Next day, fetal reduction by ultrasound-guided fetal cardiac aspiration was performed by inserting a 16 gauge Wallace Dual Lumen Oocyte Recovery needle into the thorax of the fetus to be aborted. Aspiration was repeatedly performed till cardiac activity completely stopped and observed subsequently for 3 minutes to ascertain heart beat cessation before needle withdrawal. The fetus with smallest crown-rump length, and/or that located closest to the fundus of the uterus was chosen for reduction. The procedure was repeated in 3 fetuses: two in one sac and in one of the other twin sac. Prior to discharging the patient from daycare transvaginal scanning confirmed positive cardiac activity for the second twin and for the singleton as well as absence of sub-chorionic haemorrhage. Postoperative oral antibiotics (Augmentin 375 mg three times a day) were given for 5 days. Her antenatal care was unremarkable and serial ultrasound scans were normal. When pregnancy reached 14 weeks the couple decided to return back to their country. We made regular phone calls to them and confirmed the birth of two normal healthy babies by Caesarean section at 35 weeks plus 6 days for preterm labour following an uneventful antenatal period.

## Discussion

We report, to our knowledge, on the first case of 2 sets of monozygotic twins co-existing with a singleton pregnancy resulting from transfer of three cleaved embryos in an IVF /ICSI patient. Monozygosity was diagnosed in this case as the number of fetuses (five) exceeded the number of embryos replaced (three). It is very unlikely that one or two fetuses could have resulted from a spontaneously fertilized unrecovered oocyte as the couple fully denied any intercourse around the time of IVF/embryo transfer. Moreover, out of the three sacs, there were two monochorionic monoamniotic twins.

Despite nondirective pre-conception counseling regarding fetal and maternal complications of multiple births, the couple insisted on having 3 embryos replaced. There is no legislation in Jordan limiting the number of embryos to be transferred. The medical team did not succeed to convince the couple to accept transferring one or two embryos only, in fact they were still keen to have 3 embryos replaced even though the team gave them the option to leave their embryos to the blastocyst stage. Had the couple received information regarding embryos splitting and the potential complications associated with MZT, they

probably would have accepted to have only one or two embryos at most. This case should discourage the transfer of more than one embryo even in cleavage stage transfer particularly when embryos derived from younger oocytes. We therefore call on all countries to set a legal limit on the number of embryos transferred in a single cycle

A study compared IVF and ICSI and found a significantly higher rate of monozygotic twins only after ICSI and blastocyst transfer (8.9 versus 0%; 5.9 versus 0%).<sup>[9]</sup> Mostly this is due to disruption of the mucopolysaccharide architecture of the zona pellucida. <sup>[10]</sup> Other investigators found that younger maternal age is associated with monozygotic twinning. <sup>[11]</sup> This case has therefore two risk factors which adds further support to the necessity of counseling such patients re embryo splitting in utero.

Feticide was first described in 1978 by Alberg, who performed intracardiac puncture of the fetal heart of a fetus affected by Hurler's syndrome. <sup>[12]</sup> Nonetheless, feticide gained more popularity in the last two decades to ameliorate the adverse sequelae of high order multiple pregnancies resulting from assisted reproductive technologies as in this case. Although it is debatable whether feticide is appropriate for triplets, it is generally accepted in cases of quintuplets due to the higher fetal loss rates. Our couple were counseled on the potential risks and benefits of fetal reduction to twins, or to a singleton. It was their autonomous decision to undergo reduction to twins. As both twins were monochorionic, intracardiac potassium chloride could not be used and cardiac puncture and aspiration was used instead.

## **Conclusion**

Fetal reduction of high order pregnancies remains relatively the best option to reduce the risks for the mother and her babies despite the ethical and psychological dilemmas associated with it. Patients undergoing assisted conception treatment can be at a small but definite risk of monozygotic twinning, therefore, clinicians should keep this in mind when counseling patients regarding the number of embryos to be placed.

## **Abbreviations**

MZT: monozygotic twins, IVF: In vitro fertilization, ICSI: Intra-cytoplasmic sperm injection, 2D: two dimensional.

## **Declarations**

## **Ethical approval and Consent to participate**

Consent was taken from patient for information to be used for research purposes. Ethical approval not applicable.

## **Consent for Publication**

Written consent was obtained from patient for information to be published for research purposes.

## Availability of data and material

The datasets used during the current study are available from the corresponding author on reasonable request.

## Competing of Interest

The authors declare that there is no competing of interest regarding the publication of this paper.

## Funding

Not applicable

## Author's contributions

AA and AK wrote the draft of the manuscript, NA designed and reviewed the case report as well as provided the data. All authors have read and approved the manuscript.

## Acknowledgements

Not applicable

## References

1. Yovich JL, Stanger JD, Graaug A, et al (1994) Monozygotic twins from in vitro fertilization. *Fertil Steril.* 1984 Jun;41(6):833-7.
2. Busnelli A, Dallagiovanna C, Reschini M, Paffoni A, Fedele L, Somigliana E. Risk factors for monozygotic twinning after in vitro fertilization: a systematic review and meta-analysis. *Fertil Steril.* 2019;111(2):302- doi:10.1016/j.fertnstert.2018.10.025
3. Derom C, Vlietinck R, Derom R. et al (1987) . Increased monozygotic twinning rate after ovulation induction, *Lancet* 1987 Jul 18;2(8551):170
4. Schachter M1, Raziel A, Friedler S. et al (2001). Monozygotic twinning after assisted reproductive techniques: a phenomenon independent of micromanipulation. *Hum Reprod.* Jun;16(6):1264-9.
5. Hershlag A, Paine T, Cooper GW, et al (1999). Monozygotic twinning associated with mechanical assisted hatching, *Fertil Steril* , vol. 71 (pg. 144-146)

6. Saravelos, S.H., Zhang, T., Chung, J.P.W. et al. Monochorionic quadramniotic and triamniotic pregnancies following single embryo transfers: two case reports and a review of the literature. *J Assist Reprod Genet* 33, 27–32 (2016). <https://doi.org/10.1007/s10815-015-0611-2>
7. Kaufman MH. Two examples of monoamniotic monozygotic twinning in diploid parthenogenetic mouse embryos. *J Exp Zool.* 1982;224(2):277- doi:10.1002/jez.1402240218
8. Marcus SF1, Brinsden PR, Macnamee M, etal (1993) Comparative trial between an ultra-short and long protocol of luteinizing hormone-releasing hormone agonist for ovarian stimulation in in-vitro fertilization. *Hum Reprod.*;8, 238-43
9. Tarlatzis BC, Qublan, HS, Sanopoulou T, etal (2002) Increase in the monozygotic twinning rate after intracytoplasmic sperm injection and blastocyst stage embryo transfer. *Fertil Steril* 77,196± 198.
10. Alikani M1, Noyes N, Cohen J, Rosenwaks Z.. (1994). Monozygotic twinning in the human is associated with the zona pellucida architecture *Hum Reprod.* Jul;9(7):1318-2
11. Knopman JM, Krey LC, Oh C, Lee J, McCaffrey C, Noyes N. What makes them split? Identifying risk factors that lead to monozygotic twins after in vitro fertilization. *Fertil Steril* 2014;102:82–89.
12. Alberg A, Mitelman F, Cantz M, Gehler J. Cardiac puncture of fetus with Hurler's disease avoiding abortion of unaffected co-twin. *Lancet* 1978;2:990–991

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [ScreenShot20201103at5.31.43PM.png](#)
- [ScreenShot20201103at5.32.02PM.png](#)