

R E V I E W

Combined use of medically-assisted reproductive techniques: a new bioethical issue

Matteo Bertelli¹, Stefano Paolacci², Giorgio Placidi³, Gino Scaccia^{4,5}, Pietro Chiurazzi^{6,7}, Ezio Fulcheri⁸, Daniele Malacarne², Boleslav Lichterman⁹, Paolo Petralia¹⁰

¹MAGI Euregio, Bolzano, Italy; ²MAGI's Lab, Rovereto (TN), Italy; ³Institute of Ophthalmology, Policlinico Gemelli, Catholic University, Rome, Italy; ⁴Department of Law, LUISS Guido Carli University, Rome, Italy; ⁵Department of Law, University of Teramo, Teramo, Italy; ⁶Istituto di Medicina Genomica, Università Cattolica del Sacro Cuore, Rome, Italy; ⁷UOC Genetica Medica, Fondazione Policlinico Universitario A. Gemelli, IRCCS, Rome Italy; ⁸UOSD Fetal and Perinatal Pathology, Department of Translational Research, Laboratory Medicine, Diagnostics and Services, IRCCS Giannina Gaslini Institute, Genoa, Italy; ⁹Department of Humanities, The IM Sechenov First Moscow State Medical University, Moscow, Russia; ¹⁰General Director, IRCCS Giannina Gaslini Institute, Genoa, Italy

Summary. *Background and aim:* The studies of Nobel laureate Robert Geoffrey Edwards led to the first *in vitro* fertilization and embryo transfer in 1978. Since then, reproductive medicine has made huge advances. Methods available to sterile couples now include: purchasing oocytes and sperm, uterus surrogacy, pre-implantation or pre-natal diagnosis, embryo/fetal selection. Here we highlight the fact that combinations of existing technologies could threaten the non-marketability of human life. *Methods:* We searched PubMed and websites to find articles regarding assisted reproduction techniques. *Results:* These methods, taken separately, provide support for natural fertilization, but when used together, they may lead to genuine “baby factories”. In poor countries, such “factories” exist and often act illegally. *Conclusions:* We highlight the need for deeper bioethical studies and better legislation regarding the combined use of medically-assisted reproductive techniques. (www.actabiomedica.it)

Key words: medically assisted reproduction, *in vitro* fertilization, oocyte/sperm donation, uterus surrogacy, baby factories

Introduction

Infertility is a widespread condition that affects the lives of millions of people. Since the pioneering research of Nobel laureate Robert Geoffrey Edwards led to the first *in vitro* fertilization (IVF) and embryo transfer in 1978 (1), reproductive medicine has made huge technological advances. In the first application of IVF, female infertility was the problem to solve. Oocytes were collected during a spontaneous cycle, but soon induction of ovulation became part of the treatment. In 1991, intracytoplasmic sperm injection was introduced, revolutionizing treatment in cases of male

infertility. Development of increasingly efficient techniques for freezing sperm (2), oocytes (3) and embryos (4) has made fertilization more flexible (5). Assisted reproductive techniques are now used worldwide (6). The European Society of Human Reproduction and Embryology estimated that in 2012 five million babies were born as a result of medically assisted reproduction (MAR) (7). However, problems associated with MAR are much more extensive than is apparent and few other areas of medicine have created as many social and ethical questions or have drawn as much public interest. Society is involved at cultural, religious, social, medical and legislative levels. More than any other

field of medicine, MAR and human embryo research require the support and contribution of the entire society: legislators, physicians, human rights organizations and women's representatives (8). Medically assisted reproduction, involving IVF, has raised the expectations of many infertile couples, generated an overproduction of laws and sparked many ethical and social debates (9).

The wide range of methods now available to sterile couples includes purchasing oocytes and sperm, uterus surrogacy, pre-implantation/pre-natal diagnosis on embryos or fetuses (genetic and/or echographic analysis) and selection/abortion of imperfect embryos/fetuses. These methods offer important support to natural fertilization, but in combination may give rise to genuine "baby factories". From this perspective, the main risk is replacement of medically assisted reproductive techniques with a multi-step process consisting of programmed embryo production and sale, eliminating imperfect "products". This risk should be avoided by specific laws. Here we highlight the universal bioethical issues raised by these techniques.

Purchasing oocytes and sperm

The donation of oocytes and sperm is a starting point for generating an embryo. The advent of MAR brought with it the new figure of "donors" who sell their own sperm or oocytes to customers opting for artificial insemination. The term "donor" is not exactly correct, since in many countries sperm is sold rather than donated (10).

Uterus surrogacy

Surrogate motherhood has become a widespread social phenomenon in recent years: women from various countries, such as India, Cambodia, Thailand, Eastern Europe and the USA rent out their uterus for pregnancies that eventually end with separation of the babies from their mothers for monetary compensation (11). The most controversial practice is when the surrogate mother provides both her uterus and oocytes. In this case, the couple chooses the oocyte-and-womb donor. Surrogate mothers are also checked for genetic diseases that could be inherited by the fetuses. It is obvious why these practices are becoming more and more

common in poor countries, where "labour" is abundant and cheap. These couples rent the wombs of women who have no other source of income and who live their lives in baby factories. Here they go through pregnancies on behalf of their foreign clients (12).

Pre-implantation and prenatal genetic testing

Pre-implantation diagnosis provides specific information about genetic diseases or the gender of embryos for implant. In some cases, however, even more specific characteristics can be identified, such as eye color (13,14). Prenatal genetic testing enables parents to know pathogenic variants in the fetus, in which case the aim of testing is to avoid the birth of babies with genetic diseases (15).

Discussion

Since its advent, medically assisted reproduction has developed into an industry. It has revolutionized the clinical field as well as society, which now needs to consider new bioethical issues about the value of life. Although national governments are promoting policies to control these new techniques, it is hard to limit wrong practices in poorer countries, for example Nigeria (16,17), Thailand (18) and India (19,20), where genuine procreation "factories" have sprung up. Negligence, such as absence of appropriate health-care for newborn babies, has been documented (21), as well as non-ethical practices, such as slavery, rape and violence to force women to live in these institutions (22).

Despite worldwide ethical, social and scientific debate about the medically assisted reproduction industry, to our knowledge there have been no articles on how these techniques threaten human dignity when combined in a production line (22).

Treating unborn children as goods to be traded, subject to market laws, causes a worldwide social dichotomy. A more wealthy population makes decisions about the lives of others, selecting phenotypic and genetic traits. In many cases, parents decide whether, how and when a baby should be born, and the process leading to its birth involves a purchase.

Universal regulation of medically assisted reproduction is needed to prevent violations to human dignity and should consider the inevitable consequences of leaving such clinical practices under market control. There are several examples of declarations and laws that defend human dignity against eugenic practices, such as Article 2 of the Universal Declaration on the Human Genome and Human Rights of UNESCO (11/11/1997), that states: “*Everyone has a right to respect for their dignity and for their rights regardless of their genetic characteristics*”, and “*that dignity makes it imperative not to reduce individuals to their genetic characteristics and to respect their uniqueness and diversity*”. The issue of the combined use of medically assisted reproduction techniques is not, however, addressed. One reason is certainly the complexity of the question, but this should not prevent thorough discussion at international level. For example, an attempt to deal with issues associated with commercial medically assisted reproduction has been made in India. The Surrogacy (Regulation) Bill was brought before Parliament in 2016 in response to human rights groups calling for action in the unregulated area of commercial surrogacy arrangements. Both houses of Parliament reviewed the Bill, which passed in December 2018 (23). The law seeks to protect women and children against exploitation and commodification (24).

Conclusion

Medically assisted reproductive techniques are useful in many cases, such as when a couple that wishes to have children is sterile or carries pathogenic mutations that may be lethal for their children. However, these techniques may be used in illegal and unethical ways, as in the case of the increasingly common “baby factories” in poor and developing countries. Raising awareness of these issues may help reduce the legislative gap that allows “baby factories” to flourish. In 2005, UNESCO issued a “Universal Draft Declaration on Bioethics and Human Rights” as a model for national legislations. However, different religious and political views and the need to strike a reasonable balance between scientific research, the rights of parents and newborns, and respect for life make it difficult to find a common formulation (25).

Acknowledgments

We thank Helen Ampt for English language editing.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Steptoe PC, Edwards RG. Birth after the reimplantation of a human embryo. *Lancet* 1978; 312: 366.
2. Palomar Rios A, Gascón A, Martínez JV, Balasch S, Molina Botella I. Sperm preparation after freezing improves motile sperm count, motility, and viability in frozen-thawed sperm compared with sperm preparation before freezing-thawing process. *J Assist Reprod Genet* 2017; 35: 237–45.
3. Nagy ZP, Anderson RE, Feinberg EC, Hayward B, Mahony MC. The Human Oocyte Preservation Experience (HOPE) registry: evaluation of cryopreservation techniques and oocyte source on outcomes. *Reprod Biol Endocrinol* 2017; 15: 10.
4. Roque M, Valle M, Kostolias A, Sampaio M, Geber S. Freeze-all cycle in reproductive medicine: current perspectives. *JBRA Assist Reprod* 2017; 21: 49–53.
5. Palermo GD, Neri QV, Hariprashad JJ, Davis OK, Veeck LL, Rosenwaks Z. ICSI and its outcome. *Semin Reprod Med* 2000; 18: 161–9.
6. Izzo CR, Monteleone PA, Serafini PC. Human reproduction: current status. *Rev Assoc Med Bras* 2015; 61: 1–6.
7. <https://www.sciencedaily.com/releases/2012/07/120702134746.htm> – Accessed: 19th March, 2019.
8. Dickens BM. Interactions of law and ethics affecting reproductive choice. *Med Law* 2005; 24: 549–59.
9. Vayena E, Rowe PJ, Griffin PD. Current practices and controversies in assisted reproduction. Report of a meeting on “Medical, Ethical and Social Aspects of Assisted Reproduction” held at WHO Headquarters in Geneva, Switzerland, 17–21 September 2001.
10. Klitzman R, Sauer MV. Creating and selling embryos for “donation”: ethical challenges. *Am J Obstet Gynecol* 2015; 212: 167–70.
11. Nilsson E. Merit making, money and motherhood - women’s experiences of commercial surrogacy in Thailand. Master Thesis in Gender Studies, Centre for Gender Research Uppsala University, Sweden, 2015.
12. Spar DL. The baby business: how money, science, and politics drive the commerce of conception. Harvard Business School Press, Brighton, Massachusetts, 2006.
13. Mauron A. Choosing among possible persons: the ethics of prenatal selection in the postgenomic age. *C R Biol* 2015; 338: 566–70.

14. <https://www.fertility-docs.com/programs-and-services/pgd-screening/choose-your-babys-eye-color.php> - Accessed: 19th March, 2019.
15. Traeger-Synodinos J. Pre-implantation genetic diagnosis. *Best Pract Res Clin Obstet Gynaecol* 2017; 39: 74–88.
16. Makinde OA, Makinde OO, Olaleye O, Brown B, Odimegwu CO. Baby factories taint surrogacy in Nigeria. *Reprod Biomed Online* 2016; 32: 6-8.
17. <http://www.bbc.com/news/world-africa-43905606> - Accessed: 18th March, 2019.
18. <http://www.bbc.com/news/world-asia-43169974> - Accessed: 18th March, 2019.
19. Tanderup M, Reddy S, Patel T, Bruun Nielsen B. Reproductive ethics in commercial surrogacy: decision-making in IVF clinics in New Delhi, India. *J Bioeth Inq* 2015; 12: 491–501.
20. <https://www.theguardian.com/commentisfree/2012/jun/05/india-surrogates-impoverished-die> - Accessed: 1st March, 2019.
21. Makinde OA, Olaleye O, Makinde OO, Huntley SS, Brown B. Baby factories in Nigeria: starting the discussion toward a national prevention policy. *Trauma, Violence, Abuse* 2017; 18: 98–105.
22. Makinde OA. Infant trafficking and baby factories: a new tale of child abuse in Nigeria. *Child Abuse Rev* 2015; 25: 433–43.
23. <https://www.ndtv.com/india-news/surrogacy-regulation-bill-passed-in-lok-sabha-10-points-1965215> - Accessed: 1st March, 2019.
24. Timms O. Ending commercial surrogacy in India: significance of the surrogacy (regulation) bill, 2016. *Indian J Med Ethics* 2018; 3: 99-102.
25. Busardò FP, Gulino M, Napoletano S, Zaami S, Frati P. The evolution of legislation in the field of medically assisted reproduction and embryo stem cell research in European Union members. *Biomed Res Int* 2014; 2014: 307160.

Received: 5 August 2019

Accepted: 5 September 2019

Correspondence:

Stefano Paolacci

Via delle Maioliche 57/D - 38068 Rovereto (TN), Italy

E-mail: stefano.paolacci@assomagi.org