

2014-2017. How medically assisted reproduction changed in Italy. A short comparative synthesis with European countries

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Abstract

More than ten years after law n. 40 of February 19, 2004 became effective, regulation on medically assisted reproduction has dramatically changed outlook.

The authors report on the steps that led to these changes through Courts' rulings, the Supreme Court's verdicts and the European Court of Human Rights' decisions, as well as ministerial regulations and guidelines concerning medically assisted reproduction.

The aforementioned jurisprudential evolution was set to reach a new balance between the embryo's right to its own dignity and the woman's right to health and freedom of self-determination in reproduction. No court ruling denies that embryos have also to be safeguarded. In fact, there are still numerous prohibitions, including using embryos for experimental purposes. Judges aim primarily at avoiding that embryos' rights overcome the right to parenthood.

The authors review the legislation of the various European countries: some have adopted a legislation to regulate medically assisted reproduction, while others have developed in this field some recommendations or guidelines. This is why they call for enactment of a European law governing the implementation/operational methods of medically assisted reproduction in order to avoid the scourge of procreative tourism to countries that have a more permissive law. *Clin Ter 2017; 168(4):e248-252. doi: 10.7417/CT.2017.2014*

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Introduction

Before law n. 40/2004 became effective, medically assisted reproduction (MAR) was disciplined by health ministerial regulations, provisions of the deontological code and, mainly, by Court rulings that allowed the use of specific assisted reproduction techniques.

With the aim of regulating the matter the Parliament approved the law n. 40 dated February 19, 2004 on "Rules on medically assisted reproduction"(1). MAR may be practiced only in the event of proven infertility, can be used married or

unmarried couples, of different sex, age and child-bearing age. They are, therefore, excluded gays, singles and older women. Is forbidden heterologous fertilization, that is with eggs or sperm from outside the couple and an that the post-mortem fertilization, ie the one that takes place after the death of man using his semen previously cryopreserved. The law prohibits the use of embryos for any research unless it is specifically aimed toward improving the therapeutic and medical condition of the embryo concerned. Instead, the 2004 law gives widespread support to tissue (adult) stem cell research. (2) They can be a maximum of three fertilized oocytes and these embryos must all be implanted in the uterus simultaneously. The law prohibits pre-implantation investigation. (3,4) Thirteen entry into force, many rulings of courts, the Constitutional Court and European Court of Human Rights amended the law in the least restrictive way. Let us examine them in detail.

After twelve years since the law became effective, many Constitutional and European Court judgements, step by step, have cancelled some of the most restrictive choices made by the legislator:

- 1) The prohibition of embryo cryopreservation, with the simultaneous obligation to implant a number of embryos not higher than three, was amended by Judgement n. 151, dated *May 8, 2009* (5);
- 2) heterologous fertilization prohibition was cancelled by Judgement n. 162, dated *June 10, 2014* (6);
- 3) the prohibition for fertile couples with serious genetic diseases to access MAR was removed by Judgement n. 96, dated *June 5, 2015* (7).

With Judgement *n.151/2009* (5), the Constitutional Court cancelled two of the strictest limits to MAR: the ban to produce more than three embryos and freeze the ones which have not been implanted.

Art. 14, paragraph 2, law n. 40/2004 prohibited to produce a number of embryos higher than that strictly needed for a single and contemporaneous implant, and anyhow not higher than three. This rule brought two negative results: it did not safeguard embryos' life; it impinged the right of woman to

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health by forcing her to run the risk of new cycles of ovarian stimulation every time the implant failed. According to the Constitutional Court, the law should not have imposed the general and absolute limit of three embryos, ruling out medical evaluation of the individual clinical case that in “the field of therapeutic procedures should be the basic rule”. The Court provides that gynaecologists must fertilize a number of oocytes higher than the ones needed for implant in order to have a number of zygotes large enough to increase the chances of success even in couples that produce lower quality embryos. Embryos produced, but not implanted on the basis of the physician’s decision, have to be cryopreserved. (8) Following this judgement, the number of cryopreserved embryos in MAR centres has greatly increased in recent years. However, this embryo preservation technique may also create problems due to technical problems, it is also necessary to consider this aspect (9- 11). According to data reported in the last embryos census, 3415 are the embryos for which there was a written waiver to the implant and 6079 for which it was impossible to trace the couple that had requested cryopreservation. (12) The annual surveys carried out by the Ministry of Health (art. 15, *Law n. 40/2004*) show that this judgement has changed the practice of MAR in Italy. The latest data available (13) relative to the years 2009-2012 indicate that the number of couples that underwent MAR has increased from 63.800 to 72.500, pregnancies raised from 14.000 to 15.600, and the number of alive newborns increased from 10.800 to almost 12.000. Conversely, multiple pregnancies, that accounted to 2.7% of births post MAR dropped to 1.9% in 2010 and to 1.4% in 2012. This value is still higher than the European average, which stands at about 1.0%.

Pre-implant diagnosis ban

Pre-implant diagnosis is vital to allow genetic risk couples (silent carriers of beta thalassemia, cystic fibrosis, thalassemia, Huntington disease, muscular dystrophy, homozygous familial hypercholesterolemia, Steinert disease, haemophilia, etc.) to have children not affected by the genetic disorder the parents are carriers of. Law n. 40/2004 does not explicitly prohibit pre-implant diagnosis, unless it is carried out for eugenic purposes. Conversely, it grants the couples the right to be informed on the state of health of their embryos. Pre-implant diagnosis ban was added later in the ministerial guidelines of 2004 that have established that investigations on the state of health of the embryos could be only “observational”, by that meaning that the embryo has to be affected by anomalies detectable through observation alone, allowing *de facto* only the diagnosis of morphological alterations and not genetic. (14) In this way, the legislator probably wanted to avoid that the couple could refuse the implant after the embryo’s genetic features had been disclosed. Following the Judgements of Cagliari (15) and Florence (16), even the Regional Administrative Court of Lazio (17) declared the 2004 guidelines illegal because the Ministry had gone beyond the powers conferred on it by law. The ministerial guidelines of 2008 removed the prohibition of pre-implant genetic diagnosis. (18) The currently applicable ministerial guidelines have added that

investigations on the state of health of embryos created *in vitro* have always to be directed towards health protection and development of each embryo (19).

Constitutional Court removes the ban on heterologous fertilization

The hardest hit to the law 40 occurred with the ban elimination of heterologous fertilization decided by the Constitutional Court, Judgement no. 162 of June 10, 2014 (5).

Law n. 40/2004, art. 4, paragraph 3, provided the absolute prohibition to access heterologous fertilization. In fact, it discriminated infertile couples, unable to procreate through homologous fertilization, due to infertility of one of the two subjects, compared to the fertile ones that could procreate through homologous fertilization, and discriminated couples that for the lack of economic resources could not go abroad to access heterologous fertilization (20).

The Courts of Milan, Florence and Catania, by orders of *April 8 March 29 and April 13, 2013* (21- 23) asked the Constitutional Court to affirm the illegality of the heterologous fertilization ban, the only applicable treatment when one or both members of the couple are completely unable to produce usable gametes.

The Constitutional Court with Judgement n.162 of June 10, 2014 met this request. (6) In fact, it highlighted violations of the right of self-determination, as well as physical and psychological health of the couple. According to the Court, self-determination is fulfilled even in terms of the choices regarding procreation, as they affect private and family life.

Furthermore, the genetic origin is not relevant in the conception of “family”: in fact, children abandoned by their own family may be adopted and become part of the adoptive parent family (arts 74 and 315 Civil Code). Conversely, law 40/2004 protects the *conceptus* but impinges the fundamental rights of the subjects involved. The Constitutional Court challenged this decision and claimed that the protection of embryos is however not absolute, but has to be balanced with the protection of health and the right to procreate. As prohibition of heterologous fertilization has been eliminated, it has become mandatory to regulate this practice. To this end, on August 6, 2015 the Ministry of Health set up a proposal for a regulation on heterologous fertilization (24), also approved by the State-Region Conference.

The Proposal sets some limits. First, the age of donors. The age has been fixed between 18 and 40 years for men and between 20 and 35 years for women (25- 27).

The regulation prohibits the donation of gametes between relatives up to the fourth degree (for these, in fact, the risk of transmitting genetic diseases is higher) and guarantees the donor’s anonymity: the couple that accesses the heterologous fertilization receives exhaustive information on the outcome of the tests the donor has undertaken, in full respect of his/her privacy. In case of health needs, the donor can be traced through the National Registry.

The fertile couples, but carriers of genetic diseases transmissible to the fetus, may access Medical assisted reproduction

Judgement n. 162 of *June 10, 2014* (6) allowed pre-implant diagnosis to sterile or infertile couples affected by genetic diseases, but made even more distressing the condition of couples carriers of genetic diseases, but fertile. For these, in fact, the law prohibited access to MAR, and therefore also to pre-implant diagnosis, essential to identify the embryos to which the gene has not been transferred and have the chance of giving birth to a child not affected by the parents' disease. Well known is the event that led to the Constitutional Court judgment no. 96/2015: a couple, carrier of cystic fibrosis - already transmitted to one daughter, and subsequent cause of abortion - had not been authorized to *in vitro* fertilization and pre-implant diagnosis because it was "fertile." The couple therefore appealed to the European Court of Human Rights (hereinafter ECHR) claiming the right to pre-implant diagnosis in order to know beforehand if the embryo was affected by the genetic disease they were carriers of (28 - 30). The court accepted the appeal and condemned Italy (requiring the State to comply with the judgement) as it deemed that the prohibition provided for by the Italian law was irrational and overstepped the discretion limit allowed to the State by Art. 8 of the European Convention on Human Rights. Indeed, law n. 194/1978 allows interruption of pregnancy if the embryo is affected by anomalies or malformations that may seriously affect the physical or mental health of the woman. Therefore, the Court stated that it is irrational not to allow pre-implant diagnosis that, conversely, in a minimally invasive way, allows to identify healthy embryos, thus avoiding implant of those sick and, therefore, voluntary interruption of pregnancy. However, the legislator has not yet modified law n. 40, in accordance with the European Court resolution.

For this reason, some Courts (Rome Court, ord. January 15, 2014; Rome Court, ord. February 27, 2014 and Rome Court, ord. September 23, 2013 and Milan Court, ord. March 4, 2015) have appealed the Constitutional Court on the constitutional legitimacy regarding two topics: on the one hand the respect of self-determination in choices related to procreation, the principle of equality and reasonableness (sections 2 and 3 Cost.) and, on the other, the respect of health (section 32 Cost.). By Judgement n. 96 of June 5, 2015, the Court confirmed the illegitimacy, as it is unreasonable to prohibit MAR and pre-implant diagnosis to fertile couples affected by serious genetic diseases (even as healthy carriers) that, according to scientific evidence, can transmit serious anomalies or malformations to the unborn (31-33).

Constitutional Judges find that this rule violates the woman right to health without protecting the unborn, since law n.194/78 allows those couples to interrupt pregnancy (even repeatedly), certainly a more traumatic event. For this reason, fertile couples but carriers of transmissible genetic diseases can also access MAR and re-implant diagnosis.

To protect the embryo's dignity, it is still effective the prohibition to suppress it and the obligation for MAR centres to cryopreserve it indefinitely.

The prohibition to use embryos for purposes of scientific research

Florence Court (34) appealed to the Constitutional Court to declare unconstitutional the following rules of law n. 40/2004:

- a) the prohibition for couples to withdraw their consensus to implant after fertilization of the oocyte (art. 6); b) the prohibition to perform scientific research on embryos, (if supernumerary, ill or abandoned), aimed at the protection of the individual and public health. The case involved a couple that had expressed their decision not to proceed with MAR after having been advised that only one of their embryos was healthy and of "medium quality" and had asked to be allowed to donate the unused embryos for scientific research.

The Constitutional Court waited for the ECHR judgement on Parrillo case before expressing a judgement. The case concerned a widow of a police officer killed in the tragically famous Nassiriya attack who, in 2002 had resorted to MAR together with his partner getting 5 embryos which had never be implanted due to his sudden death in 2003. (35) The widow had given up the pregnancy, but appealed to her right of property, granted by Art 1 of Protocol 1 attached to the European Convention for the protection of human rights and fundamental freedoms and decided "to donate the embryos to science" for research purposes.

The European Court of Human Rights rejected the appeal judging that embryos cannot be reduced to mere own "objects". The European Court acknowledged that the decision to donate the embryos to scientific research is set by art. 8 of the European Convention as it is an expression of self-determination freedom related to private and family life, but excluded that Italian law violated the Convention. Two different positions have been reported in literature on the matter: on the one hand, some researchers state that those embryos should be used in scientific research, because a) embryos not implanted will eventually be lost; and b) scientific research can save millions of human lives. On the other hand, other authors underline that use and manipulation of human embryos in scientific research would involve their destruction. This is in contract with the concept that embryos must be considered subjects with human dignity since they are conceived.

The Constitutional Court in its judgment n. 84 of *April 13, 2016* underlines firstly that European law does not regulate this matter and leaves the single States a wide margin of high discretion. (36) Therefore, the Court declared not acceptable the appeal raised by the Court of Florence, and referred the decision to the legislator in charge of assessing through the different options, taking into consideration the majority of opinions on the matter.

State of the art in Europe

The survey on MAR in Europe presents a varied outlook. Some countries have a specific law, frequently updated as a result of advances in the field, others have relied on case laws and regulatory measures such as *ad-hoc* guidelines.

The majority of European countries, Spain, Switzerland, Portugal, France, Austria, Germany allow to access MAR only in case of pathologies to try to solve couples' infertility, after other methods have failed, or prevent transmission of serious diseases of genetic or hereditary origin to the unborn. In the United Kingdom and Switzerland the physician should take in due account the (future) interests of any child born as a result of in vitro fertilization. As far as the civil status is concerned, France, Switzerland, Sweden, Austria and Germany allow access to MAR only to heterosexual married or cohabiting couples (37).

In Spain *law 35/1988* and in Portugal law approved on November 20, 2015 have expanded the possibility to access MAR also to couples composed by two women.

Donation of sperm, oocytes, zygotes and embryos is also regulated differently in the various countries; ad example, sperm donation is allowed in Austria, Sweden, Switzerland, United Kingdom and Spain only with the wife or partner's consent and only if the man is willing to perform all the clinical analyses required. Donation of fertilized or unfertilized oocytes to be used for MAR is also subject to various limitations.

Austrian and German laws prohibit donation. In France, Spain and England unfertilized oocyte donation is allowed only if donors are married or cohabiting. In all cases a written consent to the use of their oocytes in the course of a treatment is required. Nearly all the states prohibit the insemination or donation, or both, after the death of one of the two parents (38).

Generally, European laws allow sperm freezing or storage in authorized banks until they can be implanted following the consent of the woman and, if married, of her husband, too. Surrogacy is prohibited in many countries including Italy, France, Spain, Sweden, Norway, Denmark, Germany, France and Finland. It is allowed in England but without compensation for the woman who gives her wom (39).

Discussion and Conclusions

Twelve years after its approval, law n. 40/2004 still forbids access to MAR to: a) same-sex couples; b) non-cohabiting couples; c) if a component is deceased (post-mortem fertilization) or is underage. Besides the above techniques, surrogacy, cloning, gametes marketing and production of hybrids or chimeras are still banned.

The judgements of the Constitutional Court changed the balance between embryos' protection and parenthood right.

Very restrictive rules favour the "procreative tourism", thus increasing discrimination between rich and poor people. The Ministry of Health, in order to favour the rapid start of MAR, updated the guidelines and included heterologous MAR in the Essential Levels of Assistance (ELA). Therefore, patients will not have to pay in full for MAR, and right to health will be protected uniformly throughout the national territory. Nonetheless, different technical issues, such as lack of donor gametes cells, still stall health facilities. Although in December 2014 the National Donor Register has been established to ensure gametes traceability, donors are few, especially female ones, as they have to undergo hormonal stimulation needed to produce oocytes.

Another problem that makes donating gametes in Italy so difficult is that the guidelines approved by the Conference of the Regions on September 4, 2014 (40) made the selection of potential donors much more difficult than in other countries. For example, with regard to oocyte donation, women not only have to undergo a hormonal stimulation for the oocyte production, but also a swab to exclude the presence of vaginal infections, such as *Candida* or *Chlamydia*. No other European country or the homologous fertilization techniques require this obligation, as the presence of infection does not increase the risks associated with oocytes withdrawal, nor the implantation in uterus of the ones fertilized.

The result is that, almost two years after the Constitutional Court judgement, couples that have managed to access MAR are very few and, even if the "reproductive migration" has slowed down, after such judgement it could start again.

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Declaration of Interest

The authors report no conflicts of interest.

Authors' contributions

The Authors have made substantial contributions to conception and design of the manuscript. All Authors have been involved in drafting the manuscript and revising it critically for important intellectual content and all of them have given final approval of the version to be published.

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