

**Review Article:****Moral challenges of research on embryos in pre-implantation genetic diagnosis and IVF****Leila Naseri<sup>1</sup>, Mahmoud Abbasi<sup>2</sup>, Mehrdad Hashemi<sup>3,\*</sup>**<sup>1</sup>Department of International public law, Payamenoor University, Tehran, Iran<sup>2</sup>Department of Med Law, Faculty of Medical Science, Shahid Beheshti University, Tehran, Iran<sup>3</sup>Department of Genetics, Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran\*Corresponding author: email address: [hashemi\\_mehrdad@yahoo.com](mailto:hashemi_mehrdad@yahoo.com) (M. Hashemi)**ABSTRACT**

Purposes of pre-implantation genetic diagnosis (PGD) include screening for single gene mutations for late onset disorders or susceptibility to cancer. The problematic issue is that PGD is to produce a healthy baby, causing the destruction of some embryos that have been transferred by in vitro fertilization (IVF). Some PGD embryos may be discarded because they are excess to the woman or couples' goal for family creation, and have been diagnosed as being affected by a particular genetic condition that woman/couple wish to avoid. So, the controversial issue is the destruction of embryos as a consequence of fertility treatment that raises questions on whether the moral status of an embryo of 3 days is the same as that of a born, living adult human being.

**Keywords:** discarding embryos; PGD; IVF; embryos as a person; research.**INTRODUCTION**

PGD is a procedure used before implantation to identify genetic disorders to avoid the birth of human beings with these conditions. This can prevent special certain genetic diseases or disorders from being transferred to the child [1]. PGD is used by couples who are at risk of having a child with a serious genetic condition, or in some cases, to couples who have experienced repeated miscarriage due to chromosome rearrangements such as reciprocal translocation [2]. Some object to doing research on embryos because of the chance of discarding embryos by PGD but some others accept it for any reason because they believe that embryos are too rudimentary in development to have rights or interests. The treatment goal of PGD is to produce a healthy baby; however, it entails discarding embryos which have not been selected for transfer to the women's womb for implantation [3]. The moral issue of discarding embryos in research raises many questions which are discussed here.

**RESEARCH LITERATURE**

In fact, research on embryo can contribute to the development of treatments to lengthen lives, reduce suffering, and enable parents to have a child. It is hoped that studies on embryonic stem (ES) cells, totipotent or pluri-potent cells from an initial embryo brings about techniques for induction of stem cells to form organs and tissues in vitro for transplantation [4]. This can solve the gap between the demand of organ and its supply. To enhance the rates of transplantation success, it may be feasible to create tissues genetically identical to the recipient cells, thus solving the graft rejection issue. Tissues from ES cells can be employed as 'cellular models' for studying human ailments and examining novel medicine candidates for toxicity and efficacy [5]. This decreases the need for the conduction of harmful studies on people. Research on ES cell may develop novel treatments for infertility via generating gametes, eggs and sperm, from in-vitro ES cells [6,7]. These are employed to cure

infertility in patients incapable of generating gametes since the gonads or ovaries were possibly taken away to treat cancer [8]. ES cell lines can be produced without the destruction of embryos [9, 10]. It is possible to directly generate stem cells from somatic cells through stimulating them to dedifferentiate into pluri-potent stem cells [11, 15]. Development of stem-cell inquiry to generate functional tissues from ES cell lines or IPS cells involves the destruction of embryos. Toti potent stem cells are also embryos since they possess the same developmental capacity; thus, studying stem cells without destroying the embryo is not feasible. Most embryo studies conducted in the UK attempt to enhance IVF therapies [16]. Research on the development of embryo renders beneficial data on the reasons of congenital disease and miscarriage. Some believe that it is not sensible to annihilate unwanted embryos from IVF to confirm these benefits of the treatment. Perhaps, the most prevalent reasoning is that embryos are human beings, which is a moral claim about the embryo. Stating that a being is a person means to assume the same claims, rights, and motivations for other humans in identical conditions. It is not right to kill a human for the purpose of research, regardless of the fact that other individuals hope this person will survive. People who think that embryos are independent beings extend this conclusion to embryos as well. If embryos possess the same moral condition as ordinary people, is not humanistic to let them die in the same conditions [17]. The assumption that embryos are human has, however, some unavoidable inferences. An implication is the consideration of 'embryo-rescue cases' [18- 19]. Assume that numerous embryos are created as the by-products of assisted fertility. Nevertheless, they are frozen and kept in a big warehouse, possibly due to the fact that the government hinders destructing them. Imagine that a fire has begun in the wareroom, which may harm the embryos, but also may threaten the life of an employee. You are exposed to an alternative: either you should save the unwanted embryos or save the life of the employee. It is obvious that you have to save the worker's life. On the other hand, if embryos are considered humans, you must save them as well, as it is morally expected to protect numerous persons in preference to a

worker. Thus, our considerations are probably contradictory with the perspective that embryos are humans. This hypothetical case may examine this moral insight. Nevertheless, the implication that embryos are humans has some improbable perceptions for real life. More than 50% of embryos die in the first eight weeks of pregnancy, which is known as spontaneous abortion [20, 21]. Accordingly, more than 220 million embryos die in the world annually [22]. So, if it is assumed that embryos are humans, it is concluded that more than 220 million individuals die every year as a result of spontaneous abortion; it is seven times more than the number of people who lose their lives because of cancer. Hence, we should do something to decrease this astonishing death rate. Its biological basis should be indicated, and therapeutic measures should be prioritized to inhibit it, assuming that it may be a noticeable cause of human death compared with other causes altogether [19, 22- 25]. Conceivably, preventing many spontaneous abortions is hard, so the blight that kills embryos should be prevented. However, there are many resources to prevent diseases such as acquired immune deficiency syndrome (AIDS) and cancer which kill fewer people. Two implausible inferences are pointed out regarding the assumption that embryos are humans. First, embryos may be saved in preference to other persons in cases of embryo rescue. Second, spontaneous abortion and loss of embryo should be considered a scientific priority. People who oppose these perceptions have two options. The first is to agree that embryos are not persons. If so, we cannot infer anymore that it is unsound to destroy embryos during research. The second alternative is to consider embryos as persons, but persons who presume themselves in particular conditions, with no normal right to be saved from natural or spontaneous mortalities, as sometimes, is similarly thought of the elderly. Few may think that the elderly people lack right to be saved. However, some argue that their claims to be saved are more feeble compared with those of the youth. Anything that possesses the name of a person can guarantee little moral assumption given either to embryos of human in cases of hypothetical embryo rescue or to sudden abortion. For instance, we might be negligent to any ailment killing 220 million people yearly, even if it merely kills the

elderly. Additionally, even if we endure the mortality of 220 million people from different illnesses, we would accord the same burial ritual dignity as we would accord to others. Neither of these is needed in early spontaneous abortion [19, 26]. The mere alternative is to agree that embryos are not ordinary humans. Therefore, assuming them as persons is a claim that cannot be regarded in the argument on the destruction of unwanted embryos in research studies. Even if embryos are not normal humans, there are not sufficient moral causes not to destroy them, as we may possess drastic reasons not to destroy higher animals. Furthermore, this presumption is not eliminated by intuitive responses to cases of embryo rescue and sudden abortion, as those frameworks do not consist of killing embryos intentionally, but only getting disappointed in rescuing them. It is doubted, however, if there are justifiable motives not to destroy unwanted embryos. The oral contraceptive pill, post-coital contraception, and intra-uterine contraceptive tools all annihilate some embryos. Almost 200,000 abortions are recorded yearly in Britain ([www.statistics.gov.uk](http://www.statistics.gov.uk)), which induces objections among a minority. In addition, most countries ask that surplus embryos generated by IVF must be killed after some time (10 years in the UK). This is not commonly considered as morally repugnant or a kind of capital crime. Based on reactions to presumptive cases, there are no reasonable justifications against the destruction of embryos. Imagine that a refrigerator with 1,000 unwanted embryos has collapsed on a small child and is making her die. You may rescue the child, merely via turning the fridge upside down so that the embryos come out their test tubes and die. Obviously, you must rescue the child, asserting that destructive embryo study is morally permissible, if not needed. In fact, destructive study on unwanted embryos might be identical to the case of refrigerator. For example, by performing research on 1,000 unwanted embryos, a scientist can possibly propose a cure. This research is expected to rescue one person; nevertheless, it also destroys all embryos. If it is judged that we can destroy the refrigerator case embryos, we have to also decide that it is permissible to kill the embryos in this case of research. It is hard to determine a decent view for the argument that suggests reasons for

not destroying unwanted research embryos. One popular view suggests that we must not kill beings that possess mental capacities [27]. The common aspects are sensitivity to pleasure and pain, self-consciousness, consciousness, and rationality. So, why these mental attributes do not permit us to kill?

Daily judgments by people regarding the wrongness of killing are dependent on the mental potentials of the being that is going to be killed. Most of us accept that killing protozoa, bacteria, mollusks, or insects (organisms that are non-rational, non-conscious, and insensitive to pain and pleasure) is permissible. In contrast, it is generally assumed wrong to kill dogs and pigs, which are nearly sensitive and conscious (also self-conscious) to pain and pleasure. Most individuals consider that humans lacking the crucial mental features possessed by adults also lack their claims, rights, and interests [28]. For instance, brain-dead persons in intensive-care units have considerably feeble claims to life-saving cure compared with normal living individuals when the brain dies. Everything critical to his/her life also seems to die. Even permanently unconscious individuals who do not possess the standards for the death of brain have lost their interests and claims [29]. Third, it is simple to make science-fiction stories, supporting the approach that the mental properties of a person influence the wrongness of killing. For instance, assume that it was feasible to transplant a brain of human to a sheep, preserving the personality, mental potentials, and memories. The outcome is a human mind and brain in a sheep. There will be strong reasons not to kill this being because we would think it is wrong to kill it. Also, consider a human mind with personality, memories, and mental capacities uploaded to a robot; of course it will possess the same mental features of an ordinary person. Will there be reasons not to switch this robot off? Clearly, there will be. Consider that we have reasons not to kill creatures with sensitivity to pleasure and pain, consciousness, self-consciousness, and rationality. This is consistent with the view that there is no significant reason to save embryos. Embryos have no consciousness [30, 31]. The beginning of fetal consciousness is reported to be at or after 24 weeks [32, 33, 34, and 35]. Embryos cannot have

pleasure and pain; this capability does not manifest before 16 weeks [31, 35, 36, and 37]. They are not of course self-conscious or rational. Self-consciousness develops late in pregnancy or after being born, and rationality grows later [38, 39]. Fourteen days after conception, embryos do not have even a nervous system. A second view considers a great value on membership of species [40]. Some creatures should not be killed because they are humans or some morally important species. To explain the special moral importance that they grant to being human, supporters of this perspective claim that humans have specific mentalities, such as rationality [41]. However, they justify the fact that human beings not having these features possess the same moral importance (i.e., being a member of a species with rationality is sufficient). The problem is that it is not obvious why membership of species has moral significance [42]. The attribution of beings to various species is dependent on different biological standards lacking moral relevance. Chimpanzees and humans are categorized as differing species on the basis of the fact that they are not able to generate reproductive offspring. This, however, does not justify the variations in human rights and those of the chimpanzees. In the same way, adult Australians and Americans can reproduce with one another and bear reproductive child. However, it is again unlikely that this is what determines their identical moral condition; a more desired explanation would be suitable to their similar mental characteristics [43, 44]. A third view claims that we should not destroy a creature and thus deprive it of a valuable future. Accordingly, it is probably incorrect to kill embryos because some embryos will become individuals with precious lives [45]. Unwanted embryos, however, do not have lives of value. If they are not killed in research, instead they are languished in freezers until they are killed for another reason. Killing these embryos in research will not deprive them from having a valuable future. There is a more unique view that eliminates this problem: we should not destroy an organism; if we do so, we would deprive it from a valuable future. However, this view is less attractive compared with the original one. It is not obvious what is incorrect with depriving something from a valuable life when we are sure

this future will not come over. This viewpoint has not reasonable implications. Imagine we could have dedifferentiated skin cells of an adult and then developed them into embryos and children. Therefore, skin cells can have a valuable future; this is in line with the view that it would be wrong to kill numerous skin cells that are shed away every day [42]. However, skin cells intrinsically lack the capacity for having a valuable future. They can only be transformed into organisms having this potential. However, the same can be considered regarding embryos [46]. It is discussed that embryos are not persons; there are also no sensible reasons not to destroy unwanted embryos. However, even if we are wrong, we may kill unwanted embryos in research because sometimes it is permissible to destroy beings including individuals that we have robust reasons not to kill [47, 48]. When embryos are not intended to form a family, they can possess still a certain moral value (i.e., a means for extension of knowledge and rescuing or enhancing people's lives). It is wrong to employ wanted embryos for the purpose of research. Wanted embryos are valuable for their parents. Destroying these embryos harms the parents and violates their moral claim regarding what is done to the embryos they generate [49]. Killing unwanted embryos with parents consented to their use and killing in research will not violate the parents' claims. Moreover, such embryos are not humans and do not have any feature justifying not to kill them. Even if embryos are persons or beings, it is permissible to get rid of unwanted embryos in research. For example, this is when research increases the survival rate of embryo. The argument against destructive experiment on unwanted embryos is invalidated by three aspects. In contrast, there is a robust reason for conducting such studies, pursuing which may develop medical techniques that will succeed. It is still wrong to generate embryos ending up with death in research, although it is permissible to kill unwanted embryos. It is thought that it is permissible to generate embryos by IVF, knowing the reality that some will be killed for no reason but their storage seems impractical. If it is possible to generate embryos in these conditions, it is also possible to generate embryos that would be killed in experimental studies. So, the embryos will be

destroyed to improve medical research, rather than emptying the freezer space, and they will be generated for a more valuable reason (i.e., for the improvement of medical treatments, rather than satisfying the desires of parents for having children) [50]. An argument states that, in the production of embryos for research, they are only used to benefit others, as they are not endowed any chance for survival. This problem can be simply resolved by randomly donating some embryos of research to infertile couples [50].

#### *1. PGD for histo-compatibility purpose*

In parents who have a child with Franconia anemia, PGD bring about change for birth of a healthy child and the hematopoietic stem cells derived from heath infant umbilical cord which can save the life of histo-compatibility afflicted child [51]. Carrying out PGD for having a healthy child with histo-compatibility with afflicted child was rejected as a source for donating hematopoietic stem cells for years and as yet in some countries such as Netherlands conducting PGD for determining histo-compatibility is forbidden. Number of malign and non-malign patients merely can be treated through bone marrow transplant and hematopoietic stem cells transplantation (HSCT). Since the HSCT success rate hinges on histo-compatibility extent between donor and donee and everyone has two types of HLA which is acquired half from mother and half from father. The chance of developing an embryo with compatible HLA with the afflicted child with Anemia Franconia is 25%, however, using this approach, it would be possible to transfer the embryos with full histo-compatibility with the afflicted child [52]

In contrast, the opponents of PGD use for this purpose believe that only once the embryo should tolerate the risks from this technique that it is featured by abounding advantages while use of this method doesn't include special gain for the selected embryo. However, conducting PGD and taking one or two cells from embryo in early stages of development doesn't bring about special risk for the embryo. In fact, the embryo has been selected for its genetic features in PGD and the only advantage of PDG for the selected embryo for this purpose is the gift of being alive and life since without PGD performance, that embryo wouldn't exist. [53]. Another prominent ethical

discussion in this regard is instrumental use of developed child through PGD and degrading the human honor and respect. In fact the parent intention for developing embryo is producing a source of organs or stem cell for transmitting to the afflicted child [54].

Definitively, when the parents' decision in PGD is merely for donation of tissue to afflicted child and the child itself is not respected by parents independently as an honorable human being, this decision would be morally wrong. From other side, degrading the child to a member donation bank by parents given their hefty effort for rescuing the first child seems to be unlikely.

Another reason of PGD performance opponents for HLA compatibility regards the parent intention for requesting PGD and the likelihood of this child from this technique feelings being hurt; however, the understanding that the PGD resultant child is developed from the intention of rescuing another afflicted child life can bring about feeling of satisfaction and self confidence in him, comparing with other people whose birth has no conscious intention and in fact is outcome of an accident, the donor child would feel esteem sense by perceiving its own reason of life. From other point, PGD opponents believe that parents' intention for rescuing the afflicted child leads to developing a sort of pressure and responsibility on donor, especially in case that the transplantation wouldn't be successful as in this case, the child fails to meet the parents expectations. Similarly, psychological effects of donation of bone marrow should not be neglected [55]. However, these effects hinges on conscious perception of donor child on the donation nature. At the beginning, youthfulness of the child thwarts his understanding of donation nature and its role in life donation to other; however, over time, the child would be able to understand his valuable role in life of another person [56].

#### *2. PGD for gender selection purpose*

PGD related technology in the context of diagnosis of genetic disease and gender related diseases have had significant advancement, and sex selection often is used for removing the embryos with gender dependent genetic disease; however, the use of PGD for gender selection (unnatural) of embryo is forbidden in some

countries, although this method is still done in many countries [57].

When ethical conflicts are considered about embryo sex selection this question comes to mind whether sex selection method for non-medical purpose (when sex selection is not for genetic disease prevention) is morally acceptable.

Is it morally acceptable to use this approach for establishing gender balance in family?

The proponents of using this approach believe that sex selection is among parent rights and consolidates the human autonomy and honor, and since this method doesn't entail any risk for others it is in no conflict with moral principles. Although from individual viewpoint, gender selection by parents isn't deemed as non-ethical practice, however, in the societies in which there is gender preference, sex selection can lead to gender imbalance [58]. Basically, embryo sex selection requesters for non-medical purposes are two groups. First group are those who consider the sex selection of their first child who usually (due to socio-cultural reasons) select male embryo. Second group are those that have a child and want a child with gender other than the first one [59]. Some scholars believe that PGD with non-medical purposes is considered as non-justified reason for sex selection especially if this selection takes place for the first child, leading to sex imbalance in society; moreover, PGD prevalence and sex selection of first child is ascertainment of gender preference which is common in some societies. However, sometimes in these societies having son is so important that it doesn't justify developing and extirpation of embryo at very early stages (at eight cell stage) as in the case of prohibition of this method, there would be selected abortion risk [60]. PGD use for second child sex selection is usually done for establishing gender diversity in family and many psychologists believe that parenting experiences is different with son and daughter and gender selection in this group doesn't represent sexism [59]. Now, is the tendency of parents for gender diversity (in family that doesn't mean gender preference) a sufficient reason for generating and again extirpating the embryo? Some scholars believe that if parent's tendency for sex selection in second child is so strong that inhibit them from having a child with

undesired gender, thus one should consider the sex selection as permissible in this group [61].

The opponent of PGD use for sex selection believe that attention to a special gender for any reason represents in fact the sexism and it is a violation to human rights. Basically, PGD is a technique for preventing birth of a child with genetic disease and it is definitely not merely for embryo gender and even the tendency to gender balance in family is sort of sexism.

However, the proponent of this technique's use for embryo sex selection believe that parents demand for gender selection in fact is parents' autonomy increase and heightens the parents control on family setup and balance and curtails unbridled growth of population. [62]

From another perspective, the accurate meaning of family balance is not properly clear. Accepting that family balance hinges on gender balance, one should admit that families with gender imbalance are somehow flawed. Similarly, one should notice that PGD use should not overshadow other moral principles such as equality (equality between men and women) and definitively only couples can use this technique who want a child with other gender. Nevertheless,, parents with gender selection in fact assign a special appreciation for child gender that is prior to appreciation of the child itself in psychosocial term. In fact, these parents have their own gender stereotype and have special expectation from a special gender which often leads to applying pressure and limitations on their child and sometimes the gender relation expectations and prediction cannot be fulfilled by children which may lead to heightened pressure on them [63].

In the end, given the cultural issues in some societies, gender preference is not for family balance or meeting the parents tendency to a specific gender; rather, it is for meeting the society's expectations from family and male gender selection by parents is a sort of consolidating the family social status [64] Ultimately, in such societies enacting restricting laws of embryo sex selection is not violation of self-authority principle of parents, as it is a decision based self-autonomy which is out of sway of intervening and social limitation and in the societies that there is a full preference on male

gender, the decision of couple for gender selection doesn't denote their self-authority; rather, it denotes the social compulsory forces and pressures for justifying the role of male gender [66-68].

### STUDY METHODOLOGY

This article is a review and it is developed from examining various MEDLINE sites and based on keywords PDG, medical ethics, gender selection and it is extracted from the numerous articles during recent two decades and are investigated.

### CONCLUSIONS

All embryos may have an opportunity to survive and a chance to be destructed, like ordinary IVF embryos. It is argued that it is not correct to generate embryos for research since this means generating embryos with the purpose of destroying them. By contrast, in standard IVF cases, embryos are only produced for the sake of reproduction. An undesired side effect of IVF is destruction of some embryos. This would be regarded reasonable if it were wrong to kill undesired embryos during research; however, this is not believed so. It is permissible to destroy embryos in research once they have been created, if they are unwanted and with the consent of their parents. Therefore, in creating embryos for research, they are generated to be treated in permissible ways; it is hard to infer what could be wrong with that. Embryos have a particular moral importance when they are intended to extend a family. When they are not planned for the so-called purpose, they may still have a specific moral value for extending knowledge and saving or improving people's lives.

### DECLARATION OF INTERESTS

The authors confirm no declaration declare that there is no conflict of interests.

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