

Fetal autonomy in fertilization for older women

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Abstract

One of the biggest bioethical dilemmas is when mother autonomy conflicts with that of the conceptus. Many studies have shown that fetuses develop senses during intrauterine life, allowing them to feel and react to the environment where they live. Fetuses must thus have rights to bioethical principles. Recent advances in assisted reproductive technologies have made it possible for older women to conceive. However, a woman's decisions regarding reproductive choices directly affect the fetus. Besides medical complications, bioethical dilemmas based on the "I can do it, but should I do it?" question have been raised. This systematic review critically evaluated the existing literature on fertilization for older women, especially the approach to fetal bioethics, including fetal autonomy. Most studies approach this subject from the mother's autonomy, mother and fetus health aspects, and social, legal, and governmental aspects. Only four studies found discussed the biological rights of the fetus. These studies comment on maternal autonomy involving the resulting offspring, the interests of the potential child as a child that does not yet exist, the interests of the child to be mothered by someone whose health could be impaired soon, and the rights and well-being of the future child. *In vitro* fertilization for older women requires further discussion regarding fetus autonomy.

Keywords: Personal autonomy. Maternal-fetal relations. Fertilization in vitro. Aged.

Resumo

Autonomia fetal na fertilização em mulheres de idade avançada

Um dos principais dilemas bioéticos decorre dos casos em que a autonomia materna entra em conflito com a do concepto. Diversos estudos têm demonstrado que fetos desenvolvem sentidos durante a vida intrauterina, permitindo-lhes sentir e reagir ao ambiente em que vivem. Fetos devem, portanto, ter direitos aos princípios bioéticos. Avanços recentes nas tecnologias de reprodução assistida possibilitaram que mulheres mais velhas concebam. No entanto, as decisões de uma mulher em relação às suas escolhas reprodutivas impactam o feto diretamente. Além das complicações médicas, dilemas bioéticos baseados na questão "eu posso fazer isso, mas será que eu devo fazer?" têm sido levantados. Esta análise sistemática avaliou criticamente a literatura existente sobre fertilização para mulheres de idade avançada, especialmente no que diz respeito à abordagem da bioética fetal, incluindo a autonomia fetal. A maioria dos estudos aborda essa temática a partir da autonomia materna, aspectos de saúde da mãe e do feto, assim como aspectos sociais, legais e governamentais. Foram encontrados apenas quatro estudos pautando os direitos biológicos do feto. Esses estudos discutem a autonomia materna envolvendo a prole resultante, os interesses da criança em potencial como uma criança que ainda não existe, os interesses da criança em ser criada por alguém cuja saúde pode estar prejudicada em pouco tempo e os direitos e bem-estar da futura criança. A fertilização *in vitro* para mulheres de idade avançada requer mais discussões sobre a autonomia do feto.

Palavras-chave: Autonomia pessoal. Relações materno-fetais. Fertilização in vitro. Idoso.

Resumen

Autonomía fetal en la fertilización en mujeres de edad avanzada

Uno de los mayores dilemas bioéticos surge en los casos en que la autonomía materna entra en conflicto con la del feto. Varios estudios han demostrado que los fetos desarrollan sus sentidos durante la vida intrauterina, lo que les permite sentir y reaccionar ante el entorno en el que viven. Por lo tanto, los fetos deben tener derecho a los principios bioéticos. Los avances recientes en las tecnologías de reproducción asistida han hecho posible que las mujeres mayores conciban. Sin embargo, las decisiones de una mujer con respecto a sus decisiones reproductivas afectan directamente al feto. Además de las complicaciones médicas, se han planteado dilemas bioéticos basados en la pregunta "Puedo hacer esto, pero ¿debería hacerlo?". Esta revisión sistemática evaluó críticamente la literatura existente sobre fertilización en mujeres de edad avanzada, especialmente en lo que respecta al enfoque de la bioética fetal, incluida la autonomía fetal. La mayoría de los estudios aborda este tema desde la perspectiva de la autonomía materna, aspectos de salud de la madre y del feto, así como aspectos sociales, legales y gubernamentales. Solo se encontraron cuatro estudios centrados en los derechos biológicos del feto. Estos estudios comentan sobre la autonomía materna que implica a la prole resultante, los intereses del niño potencial como un niño que aún no existe, los intereses del niño en ser criado por alguien cuya salud pronto podría verse perjudicada, y los derechos y el bienestar del futuro niño. La fertilización in vitro para las mujeres de edad avanzada requiere más discusiones sobre la autonomía del feto.

Palabras clave: Autonomía personal. Relaciones materno-fetales. Fertilización in vitro. Anciano.

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Autonomy has been one of the pillars of bioethics since its beginnings, being defined as the power of self-decision through full acknowledgement and free will 1. However, to exercise this right, individuals must have reached a level of maturity that allows them to make decisions related to themselves². All minors are affected by this and several bioethical questions can be raised. As the autonomy of minors is generally exercised by their parents, one of the biggest bioethical dilemmas is when the mother's autonomy suppresses that of the minor. The dilemma grows more complex if life before birth is considered, as well as the fact that the moral status of the fetus must have the same rights as that of a child 3.

The fetus is aware of their body. The fetus feels pain, reacts to touch, smell, and sound, and shows facial expressions in response to external stimuli⁴. For all this, the fetus has full moral rights and must be treated as a separate entity from the mother⁵. The moral status of the fetus may come into conflict with a pregnant woman's rights. The concept that the fetus is only "portio viscerum matris" is not accepted 'by the laws of many countries, except in a few situations. The fetus must be considered a patient in its own right, separate or separable from the woman in whom it gestates⁶.

Advances in assisted reproductive technologies (ART) have made it possible for older women to conceive ⁷. In parallel, ARTs have been used with increased frequency for women of advanced maternal age ⁸⁻¹⁰. However, a woman's medical decisions regarding reproductive choices directly affect the fetus. Besides medical complications, some bioethical questions have risen based on the "I can do it, but should I do it?" dilemma ^{11,12}. This review aims to critically evaluate the existing literature surrounding fertilization for older women, especially the approach to fetus bioethics, including fetal autonomy.

Method

The guidelines detailed in the Peer Review of Electronic Search Strategies (PRESS) were followed. The search process and reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

A systematic review the literature was conducted to better understand the meanings, foundations, and uses of the concept of fetus autonomy when related to fertilization for older women. First, the following research questions were formulated: "What is the meaning of fetus autonomy in bioethics?" and "What are the conflicts between maternal and fetal autonomy during fertilization for older women?".

The literature was then meticulously searched carried out in PubMed and the Virtual Health Library (VHL) Regional Portal, and on the Embase and Web of Science databases. Each portal and database required a unique search equation. The descriptors used were validated by the Health Sciences Descriptors (DeCS/MeSH) and applied in the search equations to retrieve relevant articles. The strategies used were as follows for each database:

- PubMed: ((fertilization) AND ("autonomy" OR "bioethics" OR "medical ethics" OR "morals" OR "principle-based ethics" OR "medical philosophy")) Filters applied: middle aged + aged: 45+ years, middle aged: 45-64 years, aged: 65+ years, 80 and over: 80+ years;
- VHL Regional Portal: ((fertilization) AND ("autonomy" OR "bioethics" OR "medical ethics" OR "morals" OR "principle-based ethics" OR "medical philosophy")) Applied filters: database, limit, document type;
- Embase: ('fertilization'/expOR fertilization) AND
 ('autonomy'/expOR 'autonomy' OR 'bioethics'/
 exp OR 'bioethics' OR 'medical ethics'/exp OR
 'medical ethics' OR 'morals'/exp OR 'morals'
 OR 'principle-based ethics'/exp OR 'principle-based ethics' OR 'medical philosophy'/exp
 OR 'medical philosophy') AND [embase]/lim
 NOT ([embase]/lim AND [medline]/lim) AND
 ([aged]/lim OR [middle aged]/lim OR [very
 elderly]/lim);
- Web of Science: ((fertilization) AND ("autonomy" OR "bioethics" OR "medical ethics" OR "morals" OR "principle-based ethics" OR "medical philosophy") AND (aged)).

The adopted inclusion criteria were studies with a bioethical focus, that used ethical concepts to substantiate positions or conclusions about autonomy and minimal interaction with the fetus, and studies specifically applied

to fertilization in women over 55 years old. Book chapters, guidelines, protocols, ethics policies, and codes of ethics were excluded. The snowball method and citation tracking were also employed.

The database search covered the entire indexing period until January 2024. The authors independently reviewed the titles, abstracts, and full content of the articles, following the established inclusion criteria. In case of doubts, the manuscripts were individually discussed until a consensus was reached. The selected manuscripts were then carefully analyzed, highlighting the relevant parts and main arguments.

Results

The initial search in the selected databases yielded 148 studies. After analyzing the titles and abstracts, 133 articles were excluded for duplicity and not meeting the age criteria. Of the 15 remaining manuscripts, 11 were discarded for not addressing bioethics or fetal autonomy. Thus, four articles were thoroughly analyzed, as illustrated in the flowchart (Figure 1).

In the ethics section, a detailed review of the four articles was conducted by two reviewers, with the extraction and synthesis of key arguments, which were summarized and presented in Chart 1.

Figure 1. PRISMA diagram

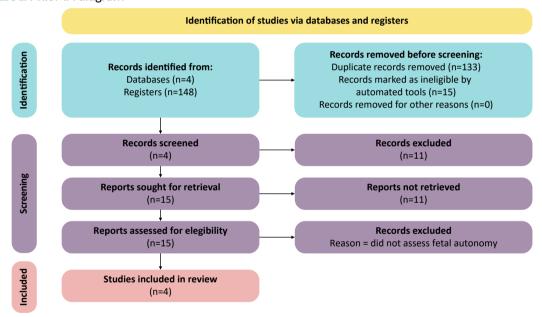


Chart 1. Ethical arguments: fetal rights and autonomy

Authorship; year; title

Bewley; 1995; "Should older women be offered in vitro fertilisation?: in vitro fertilisation is rarely successful in older women" ¹³

Cutas; 2007; "Postmenopausal motherhood: immoral, illegal? A case study" 14

Klitzman; 2016; "How old is too old? Challenges faced by clinicians concerning age cutoffs for patients undergoing in vitro fertilization" 15

Simó González and collaborators; 2016; "Pregnancy beyond 65: report of a unique case and discussion of a controversial issue" ¹⁶

Overarching theme

Consider the interests of the potential child in fact count for nothing, as the child does not yet exist then logically there would be no cases in which treatment could be refused, however old the potential parents.

It is against the interests of the child to be mothered by a person whose health is so likely to be impaired soon.

The rights and well-being of the future child—the odds of one or both parents being able to raise the child through early adulthood.

Maternal autonomy does not involve only the mother but the resulting offspring.

Discussion

This review revealed that the topic of in vitro fertilization (IVF) for older women has not yet been sufficiently addressed from the perspective of fetal bioethics. Research on fetus autonomy in the context of IVF is lacking, particularly when considering older mothers. Fetuses possess inherent rights as autonomous human entities, distinct in terms of its personality, integrity, and growth, yet reliant on its mother for sustenance and survival 17. Multiple investigations have demonstrated that fetuses have welldeveloped sensory abilities during their time in the womb 4,18. Fetuses can feel and respond to their surroundings, thereby needing the recognition of their rights, especially those based on bioethical considerations.

Bewley ¹³ argues that the interests of a potential child hold no significance, since the child does not yet exist; logically, there are no circumstances under which treatment might be denied, regardless of the age of the putative parents.

As stated by Cutas ¹⁴, children are entitled to have parents who are young, and they should also be safeguarded against more unfavorable circumstances, such as having parents who are extremely impoverished, lacking education, or belonging to a disadvantaged minority group. We agree with Cutas; yet, such conditions are socially derived, exhibit age disparities, involve biological factors, and are unaffected by human control. Essentially, it can be argued that the bioethical ideal of fairness has not been adhered to in relation to social issues like poverty.

In a study conducted by Klitzman ¹⁵, variations were observed in how IVF providers (17 physicians, 10 other providers, and 10 patients) make decisions regarding age cutoffs. These variations were related to how providers take into account the ages of the parents and the potential impact on the rights and well-being of the future child. Specifically, providers consider the likelihood of one or both parents being capable of raising the child until early adulthood. He discovered that physicians may establish age thresholds of approximately 50 years to guarantee the parents' survival until the child reaches 21 years of age. Nevertheless, other professionals do not prioritize

the child's welfare as much, primarily focusing on the mother's age as the determining factor.

Simó Gonzalez and collaborators ¹⁶ inquire whether maternal autonomy supersedes any other entitlement. They contend that maternal autonomy encompasses not only the mother, but also the offspring that is born as a result, third parties such as the attending medical team, the healthcare system responsible for the infant, and society as a collective entity. The authors argue that maternal autonomy cannot be seen as a purely individual choice.

The significance of fetal autonomy in discussions around in vitro fertilization for older women has been overlooked. Most studies primarily support the autonomy of women, focusing on economic and legal concerns. Regarding fetal autonomy, it is important to note that the fetus is not considered an adult in the foreseeable future, namely within a time frame of fewer than twenty years. Furthermore, it is uncertain if the fetus would opt to have a mother who is of the same age as its grandmother. Therefore, although in vitro fertilization appears to enhance women's liberty in various situations, it is imperative to carefully evaluate if it also compromises the autonomy and welfare of the resulting kid. There is a viewpoint that argues for a moral need to restrict older women from receiving IVF treatment due to the heightened risks for both the mother and the fetus, which are considered significant reasons for worry 19.

Advanced maternal age pregnancy poses numerous dangers to the fetus, which can extend into the postnatal period. These children have a higher likelihood of developing autistic spectrum disorders, hyperkinetic disorders, pervasive developmental disorders, Asperger's syndrome, schizophrenia, depression, and anxiety ²⁰. Furthermore, certain studies indicate a reduced lifespan for offspring born to moms of advanced age ^{21,22}. Offspring of advanced maternal age are more prone to assume a caregiving role for their parents before reaching adulthood, hence heightening the susceptibility to various illnesses.

Individuals may also experience anxiety concerning the well-being of their parents and express a dread of their parents' mortality.

Furthermore, they may struggle to become independent from their family home and exhibit a tendency to postpone pursuing higher education ²³. The approximate mortality rate of mothers who give birth to a child at the age of 50 is 15% by the time their child reaches the age of 20²⁴.

Conversely, several authors highlight the benefits associated with older parents. These individuals tend to exhibit a high level of dedication to motherhood, possess greater wisdom, and a keen understanding of the challenges that come with raising children, having observed them throughout life. Furthermore, they have had ample time to deliberate about their choice to become parents and are more inclined be financially stable ²⁵.

The contemporary advancement of academic research in biomedical ethics necessitates the execution of systematic reviews. We conducted a methodical examination of argumentative literature with the objective of providing current and thorough summaries of the ethical arguments and concepts associated with the fetus in the context of conception for older women. Several authors argue that bioethics, being a comprehensive field of philosophical investigation, is not suitable for systematic evaluation 26. For them, bioethical arguments are subjective and cannot be evaluated based on conceptions of quality and bias. Consequently, we omitted any evaluations regarding the quality of the chosen studies.

Final considerations

From this review, it may be inferred that there has been insufficient research on the topic of fetal autonomy in relation to IVF for older women. While, on the one hand, IVF for older women often enhances women's autonomy, on the other, it is crucial to carefully evaluate whether it also compromises the autonomy and well-being of the resulting human being, thus requiring further deliberation about fetal autonomy in this context.

References

- 1. Taylor RM. Ethical principles and concepts in medicine. Handb Clin Neurol [Internet]. 2013 [acesso 15 jan 2024];118:1-9. DOI: 10.1016/B978-0-444-53501-6.00001-9
- 2. Reynolds S, Grant-Kels JM, Bercovitch L. How issues of autonomy and consent differ between children and adults: kids are not just little people. Clin Dermatol [Internet]. 2017 [acesso 22 fev 2024];35(6):601-605. DOI: 10.1016/j.clindermatol.2017.08.010
- 3. Isaacs D. Moral status of the fetus: fetal rights or maternal autonomy? J Paediatr Child Health [Internet]. 2003 [acesso 5 mar 2024];39(1):58-9. DOI: 10.1046/j.1440-1754.2003.00088.x
- 4. Clark-Gambelunghe MB, Clark DA. Sensory development. Pediatr Clin North Am [Internet]. 2015 [acesso 10 abr 2024];62(2):367-84. DOI: 10.1016/j.pcl.2014.11.003
- 5. Loi M, Nobile M. The moral and legal relevance of DOHaD effects for pregnant mothers. In: Rosenfeld CS, editor. The epigenome and developmental origins of health and disease [Internet]. Amsterdam: Elsevier; 2016 [acesso 25 maio 2024]. p. 463-80. DOI: 10.1016/B978-0-12-801383-0.00023-2
- 6. Casper MJ. The making of the unborn patient: a social anatomy of fetal surgery. New Brunswick: Rutgers University Press; 1998.
- 7. Nardelli AA, Stafinski T, Motan T, Klein K, Menon D. Assisted reproductive technologies (ARTs): evaluation of evidence to support public policy development. Reprod Health [Internet]. 2014 [acesso 30 jun 2024];11(1):1-14. DOI: 10.1186/1742-4755-11-76
- 8. Moutos CP, Rasouli MA, Phelps JY. Postmenopausal pregnancy in the era of assisted reproductive technologies. Obstet Gynecol [Internet]. 2020 [acesso 12 jan 2024];136(1):154-60. DOI: 10.1097/ AOG.000000000003877

- 9. Segev Y, Riskin-Mashiah S, Lavie O, Auslender R. Assisted reproductive technologies: medical safety issues in the older woman. J Womens Health (Larchmt) [Internet]. 2011 [acesso 19 fev 2024];20(6):853-61. DOI: 10.1089/jwh.2010.2603
- **10.** Ekberg ME. Assisted reproduction for postmenopausal women. Hum Fertil (Camb) [Internet]. 2014 [acesso 1 mar 2024];17(3):223-30. DOI: 10.3109/14647273.2014.948080
- 11. Benshushan A, Schenker JG. Age limitation in human reproduction: is it justified? J Assist Reprod Genet [Internet]. 1993 [acesso 7 abr 2024];10(5):321-31. DOI: 10.1007/BF01213427
- **12.** Paulson RJ, Boostanfar R, Saadat P, Mor E, Tourgeman DE, Slater CC, *et al.* Pregnancy in the sixth decade of life: obstetric outcomes in women of advanced reproductive age. JAMA [Internet]. 2002 [acesso 20 maio 2024];288(18):2320-3. DOI: 10.1001/jama.288.18.2320
- 13. Bewley S. Should older women be offered in vitro fertilisation?: in vitro fertilisation is rarely successful in older women. BMJ [Internet]. 1995 [acesso 18 fev 2024];310(6992):1457. DOI: 10.1136/bmj.310.6992.1457
- **14.** Cutas D. Postmenopausal motherhood: immoral, illegal? A case study. Bioethics [Internet]. 2007 [acesso 8 mar 2024];21(8):458-63. DOI: 10.1111/j.1467-8519.2007.00583.x
- **15.** Klitzman RL. How old is too old? Challenges faced by clinicians concerning age cutoffs for patients undergoing in vitro fertilization. Fertil Steril [Internet]. 2016 [acesso 14 abr 2024];106(1):216-24. DOI: 10.1016/j.fertnstert.2016.03.030
- 16. Simó González M, Calaf Alsina J, Terribas Sala N, Luqui Scarcelli N, Plana Borrás J, Polo Ramos A. Pregnancy beyond 65: report of a unique case and discussion of a controversial issue. Eur J Contracept Reprod Health Care [Internet]. 2016 [acesso 26 maio 2024];21(6):496-8. DOI: 10.1080/13625187.2016.1234599
- 17. Chervenak FA, McCullough LB. Ethics in perinatal medicine: a global perspective. Semin Fetal Neonatal Med [Internet]. 2015 [acesso 28 jun 2024];20(5):364-7. DOI: 10.1016/j.siny.2015.05.003
- **18.** Lagercrantz H, Changeux JP. The emergence of human consciousness: from fetal to neonatal life. Pediatr Res [Internet]. 2009 [acesso 3 jan 2024];65(3):255-60. DOI 10.1203/PDR.0b013e3181973b0d
- 19. Caplan AL, Patrizio P. Are you ever too old to have a baby? The ethical challenges of older women using infertility services. Semin Reprod Med [Internet]. 2010 [acesso 2 jun 2024];28(4):281-6. DOI: 10.1055/s-0030-1255175
- **20.** Bergh C, Pinborg A, Wennerholm U. Parental age and child outcomes. Fertil Steril [Internet]. 2019 [acesso 6 jan 2024];111(6):1036-46. DOI: 10.1016/j.fertnstert.2019.04.026
- 21. Kemkes-Grottenthaler A. Parental effects on offspring longevity evidence from 17th to 19th century reproductive histories. Ann Hum Biol [Internet]. 2004 [acesso 11 fev 2024];31(2):139-58. DOI: 10.1080/03014460410001663407
- 22. Zhu JL, Vestergaard M, Madsen KM, Olsen J. Paternal age and mortality in children. Eur J Epidemiol [Internet]. 2008 [acesso 27 mar 2024];23(7):443-7. DOI: 10.1007/s10654-008-9253-3
- **23.** Engelhardt JA. The developmental implications of parentification: effects on childhood attachment. Grad Stud J Psychol [Internet]. 2012 [acesso 13 abr 2024];14:45-52. DOI: 10.52214/gsjp.v14i.10879
- **24.** Zweifel JE. Donor conception from the viewpoint of the child: positives, negatives, and promoting the welfare of the child. Fertil Steril [Internet]. 2015 [acesso 30 maio 2024];104(3):513-9. DOI: 10.1016/j.fertnstert.2015.06.014
- **25.** Morris C. Technology and the legal discourse of fetal autonomy. UCLA Women's Law J [Internet]. 1997 [acesso 10 jun 2024];8(1):47-97. Disponível: https://bit.ly/3TwzLCY
- **26.** Parsons JA, Johal HK. In defence of the bioethics scoping review: largely systematic literature reviewing with broad utility. Bioethics [Internet]. 2022 [acesso 17 jun 2024];36(4):423-33. DOI: 10.1111/bioe.12991

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