



The influence of endometrial thickness on embryo transfer: Literature review



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ABSTRACT

Infertility affects millions of couples around the world, and is considered a significant challenge to global health. Even after 12 months of attempts without contraception, many fail to conceive, which highlights the importance of assisted reproductive techniques as a viable solution. Over the years, several approaches have been developed to increase the chances of successful fertilization, with embryo transfer being one of the most used. However, the success of this procedure can be influenced by multiple factors, including endometrial thickness. This study aims to explore the impact of endometrial thickness on embryo transfer and its relationship with the clinical evolution of oocytes. The research consists of a narrative review of the last 10 years of literature, resulting in the in-depth analysis of 5 articles selected from 147 initial findings. The results indicate that endometrial thickness not only affects embryo transfer and oocyte development, but may also be associated with gestational complications, such as hypertensive disorders in pregnancy.

Keywords: Infertility, Assisted Reproduction, Endometrial Volume, Medicine.

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INTRODUCTION

The World Health Organization (WHO) recognizes infertility as a global public health problem, affecting about 17.8% of the world's population. Statistics reveal that approximately one in five couples of reproductive age face difficulties in conceiving, requiring specialized interventions, such as assisted reproduction techniques (PAHO/WHO, 2023). In Brazil, the Brazilian Society of Assisted Reproduction pointed out that about 8 million couples seek treatments to deal with infertility, which can result from a variety of causes, both male and female (SBRA, 2019).

Infertility is defined as the inability to conceive after 12 months of regular, unprotected sex (Cao *et al.*, 2020). To address this issue, Assisted Human Reproduction (HRA) techniques have emerged, which intervene in the natural process of reproduction to help couples who wish to fulfill the dream of motherhood or fatherhood (Zurawski; Trott, 2019). The main techniques include intrauterine artificial insemination and in vitro fertilization (IVF), which encompasses both classic IVF and intracytoplasmic sperm injection (ICSI). Since the birth of the first baby conceived by IVF in 1978, more than 7 million children have been born thanks to these techniques (Sciorio; Tramontano; Catt, 2020).

In recent decades, RHA has advanced significantly, with the development of new technologies, such as preimplantation genetic diagnosis and cryopreservation, which have contributed to increased success rates (Vander Borgh; Wines, 2018). However, birth rates by embryo transfer still do not exceed 50%, which highlights the importance of optimizing this process. Current research focuses on understanding the crucial role of the endometrium in embryonic receptivity, considering the synchrony between the embryo and the endometrium (Chen; Chen; Ho, 2020).

The study was justified since the endometrium plays a key role in the success of RHA techniques, especially in embryo transfer. Morphological aspects, such as endometrial thickness, are determinant in the receptivity of the embryo and its development. Recent studies have explored the influence of these endometrial features on the success of RHA (Nácul; Maciel; Carvalho, 2023).

In view of this scenario, this study aims to investigate the impact of endometrial thickness on embryo transfer, analyzing its relationship with the clinical evolution of oocytes and identifying uterine anatomical patterns that may interfere with the success of assisted reproduction techniques.

METHODS

This scientific investigation is a qualitative and descriptive literature review, focusing on the correlation between endometrial thickness and the clinical outcome of oocytes transferred through assisted reproduction procedures. The bibliographic search was conducted in renowned academic repositories, including Scielo, PubMed, BVS/Lilacs and Capes Journals. The descriptors used for the

search included: "Endometrium", "Endometrial thickness", "Assisted Reproduction" and "Embryo transfer".

The methodological protocol for the selection of bibliographic sources followed strict inclusion criteria, namely: full availability of the manuscript, language of publication restricted to Portuguese or English, time delimitation of publications between 2014 and 2024, relevance of the title in relation to the established descriptors, in addition to a careful evaluation through classificatory reading of the abstracts and full analysis of the texts.

On the other hand, the following exclusion criteria were established: articles with limited availability to the abstract, publications in languages other than Portuguese and English, titles incongruent with the predefined descriptors, and content that did not present substantial relevance to the scope of the research.

This methodological approach allowed a comprehensive and in-depth exploration of the specialized literature, providing a critical and reflective synthesis on the current state of knowledge on the subject in question. The narrative review, as a qualitative and descriptive study modality, enables the identification of trends, gaps and future perspectives in the field of assisted reproduction, with emphasis on the relationship between endometrial thickness and the success of oocyte transfer procedures.

RESULTS AND DISCUSSION

The initial bibliographic prospection in the scientific databases resulted in a preliminary corpus of 147 publications. However, after the implementation of a meticulous screening process, which involved the application of previously established eligibility criteria, followed by a critical and exhaustive analysis of the contents, the final scope of the review was refined to include only five studies that demonstrated precise alignment with the guiding objectives of this investigation.

The studies that met the inclusion criteria and were selected to compose the analytical core of this review are systematized in Chart 1 of results. This synoptic matrix was developed with the purpose of summarizing the essential characteristics and key findings of each article, thus facilitating a comparative analysis and an integrative synthesis of the extracted data.

Table 1. Articles included for review.

TITLE	AUTHOR/YEAR	OBJECTIVE	KEY FINDINGS
Endometrial thickness of less than 7.5 mm is associated with obstetric complications in fresh IVF cycles: a retrospective cohort study.	(Oron <i>et al.</i> , 2018)	The study aimed to evaluate the risk of obstetric complications in singleton live births resulting from fresh embryo transfers, comparing patients with endometrial thickness less than 7.5 mm and with 7.5 mm or more.	The findings of the study indicate that a thin layer of the endometrium, with a thickness of less than 7.5 mm, is associated with obstetric complications and may be linked to problems of inadequate placentation. This condition is correlated with a higher risk of complications during pregnancy.
Endometrial thickness is associated with incidence of small-for-gestational-age infants in fresh in vitro fertilization-intracytoplasmic sperm injection and embryo transfer cycles.	(GUO <i>et al.</i> , 2020)	The study aimed to investigate whether endometrial thickness (EMT) is associated with adverse obstetric and neonatal outcomes in IVF/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) cycles.	The study reveals that after IVF or ICSI with fresh embryo transfer, the risk of intrauterine growth restriction (SGA) was twice as high in women with endometrial thickness (EMT) of ≤ 7.5 mm, compared to those with EMT greater than 12 mm.
Association between endometrial thickness and birth weight in fresh IVF/ICSI embryo transfers: a retrospective cohort study of 9273 singleton births	(Liu <i>et al.</i> , 2021)	The objective of this study was to understand the association between endometrial thickness and weight of those born via ICSI embryo transfer.	The research identified that the presence of a thinner endometrium is related to lower birth weights, as indicated by neonatal weight scores, and an elevated risk of intrauterine growth restriction (CIR). Therefore, pregnant women with thin endometrium should receive specialized follow-up during pregnancy to prevent possible complications.
Endometrial thickness is not predictive for live birth after embryo transfer, even without a cutoff	(Shakerian <i>et al.</i> , 2021)	It aimed to investigate the predictive value of endometrial thickness (EMT) for live births when a lower EMT threshold is not employed for embryo transfer (ET).	According to the results of the study, endometrial thickness (TMS) was not predictive of live infant birth in fresh or frozen-thawed embryo transfer cycles. Even after excluding factors such as intracavitary pathology and inadvertent exposure to progesterone, women with thinner TMS should not be underestimated, as their potential to generate live births is comparable to that of those with thicker TMS.
The Effect of Endometrial Thickness on Pregnancy, Maternal, and Perinatal Outcomes of Women in Fresh Cycles After IVF/ICSI: A Systematic Review and Meta-Analysis.	(Liao <i>et al.</i> , 2021)	The study aimed to elucidate the effect of endometrial thickness on pregnancy, maternal and perinatal outcomes of women in fresh cycles after IVF/ICSI.	The results of the review indicate that a thin endometrium not only had a negative impact on pregnancy outcomes, but was also associated with an increased risk of hypertensive disorders of pregnancy (HPD) and intrauterine growth restriction (SGA), as well as a reduction in birth weight for babies. On the other hand, a thicker endometrium demonstrated no adverse effects on IVF outcomes.

Source: Data obtained from the chosen databases (2022).

INFLUENCE OF ENDOMETRIAL THICKNESS ON THE SUCCESS OF ASSISTED REPRODUCTION

The success of human assisted reproduction is affected by a number of factors, ranging from the individual characteristics of patients to the techniques used. One crucial factor that has received attention is the thickness or volume of the endometrium, which plays a significant role in embryo transfer and development (Dos Santos, 2018). Endometrial thickness can directly impact the

receptivity of the uterus and, consequently, the success of the fertilization procedure. Studies suggest that an inadequate endometrium can compromise embryo implantation and pregnancy maintenance, highlighting the importance of monitoring this parameter during treatment (Guo *et al.*, 2020; Liao *et al.*, 2021; Morales, 2024).

IMPACT OF THIN ENDOMETRIUM ON EMBRYO TRANSFER SUCCESS RATES

It was noted earlier that Dain *et al.*, (2013), the success of embryo transfer depends not only on the quality of the embryo, but also on uterine receptivity, and an anatomical condition called thin endometrium can lead to complications in the progression of pregnancy. Although Dain's study showed no significant differences in the long-term success rate, the issue of thin endometrium remains a major point of debate. Additional studies may offer more detailed insights into how endometrial thickness influences gestational development and the need for adjustments in clinical practices to improve outcomes.

According to Oron *et al.*, (2018), an analysis of 5,546 embryo transfer cycles revealed that endometrium with a thickness of less than 7.5 mm is associated with an increased risk of poor placentation. This condition can result in improper embryo development and further complications for the woman. Poor placentation can lead to serious problems during pregnancy, such as restricted intrauterine growth and complications related to hypertension. Early identification and monitoring of patients with thin endometrium is essential to minimize these risks and improve pregnancy outcomes.

RECOMMENDATIONS FOR PREGNANT WOMEN WITH THIN ENDOMETRIUM

Research by Liu *et al.*, (2021) suggests that in cases of thin endometrium, newborns may have lower gestational development, known as intrauterine growth restricted (SGA). It is recommended that pregnant women in the process of assisted reproduction receive special attention when there is the identification of thin endometrium. However, Shakerian *et al.*, (2021) indicate that, although an endometrium smaller than 7.5 mm is not predictive for live births in fresh or frozen-thawed embryo transfer cycles, treatment should not be neglected or interrupted. Careful management and continuous monitoring are crucial to optimize fertilization results.

To improve assisted reproduction outcomes, it is essential to perform a detailed endometrial evaluation to identify the characteristics of the endometrium and the potential risks associated with its thickness. Different assessment techniques, such as ultrasound and hysteroscopy, can help in the early identification of problems and the implementation of strategies to minimize complications (Goldberg, 2018; Zurawski; Trott, 2019). Careful monitoring can help ensure that the clinical evolution of oocytes is not compromised and that pregnant women receive the necessary support for a positive outcome.

The debate over the influence of endometrial volume on assisted reproduction presents divergences between different studies, with most robust studies indicating that thin endometrium has a detrimental effect on pregnancy and embryo transfer success. The systematic review with meta-analysis performed by Liao *et al.*, (2021) suggests that, in addition to adverse effects on pregnancy and embryo transfer, thin endometrium is also associated with an increased risk of hypertensive disorders of pregnancy. Thus, there is a need for further cohort studies and detailed investigations remains crucial to clarify and elucidate the impact of endometrial thickness on assisted reproduction.

CONCLUSION

In conducting the present narrative review of the literature, it was evident a significant scarcity of national studies on the subject in question in the databases consulted. On the other hand, the international literature presented a more robust collection of pertinent investigations. The critical analysis of the selected studies revealed a consensus among researchers regarding the substantial influence of endometrial volume, not only on the success of embryo transfer and development, but also on the incidence of associated pathologies. The need for increased vigilance in patients with endometrial thickness of less than 7.5 mm is highlighted, which is a critical parameter for reproductive prognosis.

In turn, endometrial evaluation emerges as a crucial tool in the prevention of intrauterine growth restriction (IUGR) and other gestational complications. However, a significant gap was observed in the specific recommendations for its clinical application, both in the articles analyzed and in the broader literature. The guidelines found tend to be generalist, often limited to suggesting more intensive prenatal care, without detailed protocols for the use of endometrial measurement as a predictive marker.

In view of this panorama, there is an urgent need to foster additional research focused on this theme. Prospective studies investigating the correlation between different ranges of endometrial thickness and specific reproductive outcomes could provide valuable insights for the improvement of assisted reproduction techniques. In addition, the development of evidence-based clinical guidelines for the evaluation and management of the endometrium in IVF cycles could standardize clinical practice and potentially improve treatment success rates.

The conclusion this review not only synthesizes current knowledge about the relationship between endometrial thickness and reproductive success, but also underlines the importance of expanding the body of evidence in this field. The development of specific protocols for endometrial evaluation and their systematic integration into assisted reproduction processes represent a promising frontier for the optimization of clinical outcomes and the advancement of reproductive medicine as a whole.



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