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THE ROLE OF OOCYTE IN DETERMINING FERTILIZATION SUCCESS AND EMBYO QUALITY IN VITRO FERTILIZATION (IVF) PROGRAMS

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ABSTRAK

Tujuan penelitian mengkaji peran morfologi oosit dalam menentukan keberhasilan fertilisasi dan kualitas embrio pada program fertilisasi in vitro (IVF). Penelitian ini merupakan sistematika review yang bersifat deskriptif kualitatif dengan pendekatan naratif. Data diperoleh dari literatur sekunder berupa artikel ilmiah dari jurnal nasional dan internasional bereputasi yang diakses melalui PubMed, Scopus, ScienceDirect, SpringerLink, dan Google Scholar. Morfologi oosit memainkan peran penting sebagai indikator awal dalam menentukan keberhasilan fertilisasi dan kualitas embrio dalam program fertilisasi in vitro (IVF). Berbagai parameter morfologi seperti homogenitas sitoplasma, keberadaan vakuola, penampilan badan kutub, struktur zona pelusida, ruang perivitellin, dan granularitas sitoplasma telah terbukti berkorelasi dengan potensi perkembangan embrio. Namun, morfologi oosit sendiri tidak dapat memberikan prediksi yang sepenuhnya akurat karena keterbatasan termasuk subjektivitas dalam penilaian, variabilitas antar individu, dan pengaruh faktor lingkungan laboratorium. Evaluasi visual konvensional morfologi oosit memberikan kontribusi awal yang penting tetapi masih perlu didukung oleh pendekatan lain, seperti analisis molekuler, penilaian fungsi mitokondria, dan teknologi modern seperti pencitraan selang waktu dan kecerdasan buatan. Morfologi oosit bukan satu-satunya penentu keberhasilan IVF, ia tetap merupakan komponen penting dalam strategi seleksi gamet. Penelitian lanjutan dengan pendekatan multidisipliner sangat dianjurkan untuk mengintegrasikan aspek morfologi, molekuler, dan klinis guna meningkatkan kualitas dan efektivitas layanan fertilitas di masa depan.

Kata kunci **:** embrio, *fertilisasi in vitro*, morfologi, oosit

ABSTRACT

The aim of this study is to examine the role of oocyte morphology in determining fertilization success and embryo quality in in vitro fertilization (IVF) programs. This study is a systematic review with a descriptive qualitative design using a narrative approach. Data were obtained from secondary literature in the form of scientific articles published in reputable national and international journals accessed through PubMed, Scopus, ScienceDirect, SpringerLink, and Google Scholar. Various morphological parameters such as cytoplasmic homogeneity, presence of vacuoles, polar body appearance, zona pellucida structure, perivitelline space, and cytoplasmic granularity have been shown to correlate with embryonic developmental potential. However, oocyte morphology alone cannot provide fully accurate predictions due to limitations including subjectivity in assessment, inter-individual variability, and the influence of laboratory environmental factors. Conventional visual evaluation of oocyte morphology provides an important initial contribution but still needs to be supported by other approaches, such as molecular analysis, mitochondrial function assessment, and modern technologies like time-lapse imaging and artificial intelligence. While oocyte morphology is not the sole determinant of IVF success, it remains an essential component in gamete selection strategies. Further research with a multidisciplinary approach is strongly recommended to integrate morphological, molecular, and clinical aspects in order to improve the quality and effectiveness of fertility services in the future.

Keywords ***:** embryo, morphology, oocyte, in vitro fertilization*

INTRODUCTION

Infertility is one of the major challenges in reproductive health worldwide, impacting the psychological, social, and economic well being of couples of reproductive age (Bui et al., 2024;

Ellyzabeth Sukmawati & Titi Alfiani, 2025). According to the World Health Organization (WHO), approximately 10 to 15 percent of couples globally are affected by fertility disorders (Biggs et al., 2024; Ellyzabeth Sukmawati, 2024). Alongside advances in reproductive medicine, various methods for treating infertility have been developed, among which Assisted Reproductive Technology (ART) stands out, with in vitro fertilization (IVF) being one of the most commonly used techniques (Asplund, 2020). IVF offers a chance for infertile couples to conceive by fertilizing an oocyte outside the female body under laboratory conditions (Huang et al., 2024).

The success of IVF is influenced by numerous factors, both patient-related and technical. One of the most critical biological components in the IVF process is the oocyte or egg cell. Oocyte quality is considered a key determinant throughout the reproductive stages, from fertilization and cell division to embryo formation and implantation. Therefore, oocyte assessment plays a vital role in predicting fertilization success and embryo quality in IVF programs (Ferrell et al., 2024). One widely used approach for assessing oocyte quality is morphological evaluation (Ghidini et al., 2022). This assessment is based on physical characteristics observable under a microscope, including cytoplasmic appearance, the shape and size of the polar body, the zona pellucida, the presence of vacuoles, and cortical granule structure. Oocyte morphology is typically evaluated immediately after follicular aspiration and prior to in vitro fertilization. This non-invasive and rapid method is commonly employed in IVF laboratory practice (Felix et al., 2022).

Numerous studies have shown that oocyte morphology is significantly associated with fertilization rates and the formation of high-quality embryos (Wang et al., 2020). Oocytes with normal morphology characterized by homogeneous cytoplasm, symmetrical zona pellucida, and an intact, singular polar body tend to have a higher potential for successful fertilization and development into viable embryos (Aldemir et al., 2020). Conversely, oocytes exhibiting abnormal morphology, such as large vacuoles, uneven granulation, or cytoplasmic fragmentation, are often linked to reduced fertilization rates, abnormal embryonic development, and implantation failure (Alshehre et al., 2021). In clinical practice, oocytes deemed morphologically poor are often deprioritized or excluded from fertilization (Zhang et al., 2022). However, in some cases, oocytes with suboptimal morphology have still been able to fertilize and develop into transferable embryos. This suggests that oocyte morphology should not be considered the sole determinant of embryo quality, but rather one of multiple parameters requiring a comprehensive evaluation. Thus, further investigation is needed to assess the validity of oocyte morphology as a predictor of IVF success (Morimoto et al., 2023).

In recent years, technological advancements in embryology have made oocyte and embryo assessments more objective and accurate (Li et al., 2018). For example, time-lapse imaging allows continuous monitoring of embryo development and provides more dynamic information than traditional static morphology assessments. Additionally, molecular approaches such as gene expression analysis and metabolic profiling have begun to be applied to offer more comprehensive insights into oocyte quality. Nevertheless, morphological evaluation remains the primary method for selecting oocytes for fertilization (Wang et al., 2020). The development of automated systems and machine learning algorithms for analyzing oocyte morphology images is an emerging research area in clinical embryology. This review aims to contribute to the enhancement of IVF service quality and support the development of more objective, effective, and evidence-based oocyte selection methods (Karavani et al., 2021). The success of IVF programs remains the primary hope for couples facing infertility. However, IVF success rates are still variable and tend to be low, especially among couples with advanced age or poor gamete quality. One of the most crucial aspects of the IVF process is the selection of oocytes with high potential for fertilization and development into high-quality embryos. To date, visual morphological assessment remains the main and simplest method for oocyte selection. Although it is non-invasive and relatively quick, it remains subjective and has not been consistently proven to predict IVF outcomes such as fertilization rates, embryo development, and implantation success (Muharam & Firman, 2022).

Studies specifically examining the relationship between oocyte morphology, fertilization rates, and embryo quality are of high importance. Valid and updated scientific information regarding the link between oocyte morphological characteristics and IVF outcomes is essential for clinical decision-making. Especially in an era of increasing demands for efficiency and personalized fertility care, a deeper understanding of morphological parameters can enhance the accuracy of oocyte selection and improve overall IVF success rates. Additionally, this topic is important because oocyte morphology is often used as a basis for fertilization decisions without strong scientific support or a standardized international consensus (Meneghini et al., 2023). Therefore, a systematic and critical literature review on this topic is urgently needed not only to develop best-practice recommendations for IVF laboratories but also to serve as a foundation for future improvements in objective oocyte assessment methods. The novelty of this review lies in its comprehensive and critical approach to examining the relationship between oocyte morphology and two key IVF outcomes fertilization rate and embryo quality that are often studied separately in previous research.

This review integrates recent findings from various clinical and experimental studies exploring the association of oocyte morphological components such as cytoplasmic quality, polar body characteristics, zona pellucida, vacuoles, and cortical granules with overall IVF outcomes, including embryo implantation potential and pregnancy prediction

METHOD

This study is a systematic descriptive qualitative literature review using a narrative approach. The primary aim of this review is to analyze the relationship between oocyte morphology and fertilization success as well as embryo quality in in vitro fertilization (IVF) programs. The data used in this research were obtained from secondary sources in the form of scientific articles published in reputable national and international journals. The selected articles were sourced from several trusted academic databases, including PubMed, Scopus, ScienceDirect, SpringerLink, and Google Scholar. The literature search focused on publications from 2015 to 2025 to ensure the relevance and currency of the information. Search strategies were carried out using keywords relevant to the research topic, such as “oocyte morphology,” “fertilization rate,” “embryo quality,” “IVF outcomes,” and “cytoplasmic abnormalities in oocytes.” Keyword combinations were refined using Boolean operators such as AND and OR to obtain more specific results. Articles were selected based on inclusion criteria, namely articles that directly discussed the relationship between oocyte morphology and fertilization rate and/or embryo quality, were available in English or Indonesian, and provided full-text access. Articles that only discussed embryo morphology without a connection to oocytes, were not available in full-text, or were editorials and opinion pieces without primary research data, were excluded from the analysis.

The selection process was conducted systematically by reading the titles, abstracts, and subsequently the full texts of articles that met the initial criteria. Articles that passed the screening were then analyzed in depth, focusing on the research methods used, the specific oocyte morphology parameters assessed, findings related to fertilization and embryo development, and the conclusions drawn by the authors. Data were analyzed using a descriptive qualitative technique, in which information obtained from various studies was compiled and compared to identify patterns, discrepancies, or consistency across findings. The results were then presented in thematic narrative form to illustrate each study’s contribution to the understanding of the relationship between oocyte morphology and IVF success. To improve the validity of the review, source triangulation was performed by comparing articles from various journals with different research designs. Special attention was given to experimental and observational studies with valid methodologies and sufficient sample sizes. Through this approach, the review aims to provide a comprehensive, objective, and relevant overview of the role of oocyte morphology as a potential indicator for predicting fertilization success and embryo quality in IVF programs.

RESULT

The literature review shows that oocyte morphology plays a significant role in determining outcomes in in vitro fertilization (IVF) programs, particularly regarding fertilization success and the resulting embryo quality. From the 20 articles reviewed, the majority of studies reported a significant correlation between specific oocyte morphological parameters and IVF success rates (As'adi & Sari, 2021). The most frequently analyzed morphological components in the literature include cytoplasmic quality, the presence of vacuoles, cytoplasmic granularity, polar body abnormalities, zona pellucida structure, and perivitelline space characteristics (Prabowo et al., 2022).

DISCUSSION

The cytoplasmic characteristics of the oocyte are a key indicator in morphological assessment. Oocytes with homogeneous cytoplasm and no visible vacuoles or abnormal granules generally show higher fertilization rates and better embryo development. Large vacuoles in the cytoplasm are negatively correlated with cleavage rates on day three and blastocyst formation. Vacuoles may reflect organelle damage or cytoplasmic maturation issues, which can interfere with pronucleus formation after fertilization (Aldemir et al., 2020). Abnormalities in the polar body (PB), especially the first PB, are also associated with fertilization outcomes. Oocytes with fragmented or irregular PBs tend to be of lower quality. PB fragmentation is often linked to errors in meiotic division, which directly impacts the genomic integrity and developmental potential of the oocyte. A study by Ebner et al. (2015) supports this finding, showing that oocytes with abnormal PBs had significantly lower fertilization rates than those with normal PBs (Peng et al., 2024).

The structure and thickness of the zona pellucida can affect sperm penetration during fertilization. Although still debated, some researchers suggest that an overly thick or poorly structured zona pellucida may indicate oocyte immaturity (Wassarman & Litscher, 2022). Furthermore, a large or debris-filled perivitelline space is also associated with lower fertilization outcomes, as it may reflect disorganization during ovulation or suboptimal laboratory handling (Moros-Nicolás et al., 2021). Cytoplasmic granularity, especially when uneven or centralized, is another important indicator of oocyte quality. Centralized granularity is strongly associated with reduced fertilization rates and increased fragmentation in day-3 embryos. This condition may signal intracellular maturation defects, metabolic imbalance, or mitochondrial dysfunction (Ellenburg et al., 2020). Several studies also emphasize the importance of the morphological assessment method used in the lab. While visual evaluation by embryologists is practical and quick, it remains subjective and depends on the observer's experience. Therefore, time-lapse imaging and artificial intelligence-based approaches are being developed to evaluate oocyte and embryo quality more objectively. These technologies continuously monitor embryonic development from its earliest stages, allowing for more accurate predictions based on initial oocyte morphology (Weatherbee et al., 2021).

However, not all studies find consistent correlations between oocyte morphology and IVF outcomes. Despite morphological differences, successful fertilization and embryo development were still possible, especially when intracytoplasmic sperm injection (ICSI) was used. In such cases, the fertilization technique may compensate for poor oocyte morphology. This raises questions about the validity of morphology as a sole predictor of IVF success. Additionally, other factors such as patient age, sperm quality, ovarian stimulation protocols, and the culture environment also play critical roles in IVF outcomes. Therefore, oocyte morphology should be considered as one of many parameters within a multidimensional approach to predicting IVF success (Redó-Riveiro et al., 2024). Although oocyte morphology provides valuable insight into the potential for IVF success, it should be combined with clinical data and supportive technologies to achieve optimal outcomes. This review also highlights the need for standardized oocyte morphology assessment and the development of objective, digital-based evaluation systems that can be widely implemented across fertility labs (Uk et al., 2022).

Oocyte morphology has long been used as an early indicator in fertility labs to estimate embryo development potential. However, it should be understood that morphology is not merely a superficial characteristic it reflects the biological and physiological complexity occurring during oogenesis (Magaton et al., 2023). Deeper understanding of morphological components and their impact on IVF outcomes can aid in oocyte selection optimization and potentially guide early interventions for gamete quality improvement (Guimarães et al., 2021). One morphological aspect currently gaining attention in modern research is the mitochondrion, the primary energy-producing organelle in oocytes. Although mitochondria cannot be directly observed through routine morphological assessment, cytoplasmic abnormalities such as granularity, vacuoles, and centralized granules often reflect underlying mitochondrial dysfunction. Poor mitochondrial performance results in low energy production, impairing spindle formation during meiosis and affecting chromosome segregation. This can lead to aneuploidy and failed embryo development. Therefore, cytoplasmic condition may serve as an indirect indicator of mitochondrial status (Uk et al., 2022).

Cytoplasmic granule centralization, characterized by the accumulation of dark granules in the center of the cell, is a common finding often associated with poor embryo quality. Several studies suggest that this condition not only disrupts normal oocyte maturation but may also trigger redox imbalance, oxidative stress, and DNA damage. Unfortunately, in some laboratories, this feature is still often overlooked or variably classified, highlighting the need for global standardization in morphological assessment. A deeper discussion should also focus on the zona pellucida (ZP), the glycoprotein layer surrounding the oocyte, which plays a critical role in fertilization. The structure and thickness of the ZP can affect the sperm's ability to penetrate and fertilize the oocyte. In oocytes that undergo abnormal maturation, the ZP may experience premature hardening or thickening, which impedes sperm penetration. Although ICSI techniques can technically overcome this barrier, ZP abnormalities still indicate that the oocyte may not be physiologically mature, potentially impacting embryo development quality despite successful fertilization (Murugappan et al., 2015).

In the context of the perivitelline space (PVS), the presence of debris or small fragments between the zona pellucida and the oocyte membrane is often considered a sign of degeneration or stress during ovulation. Some researchers interpret debris in the PVS as remnants of abnormal enzymatic activity or structural damage, which may interfere with oocyte activation post-fertilization. While some oocytes with PVS debris can still be fertilized, their success rates in forming blastocysts and achieving implantation tend to be lower. It is also noteworthy that current oocyte morphology assessment remains highly subjective. Unlike embryo-stage assessments, there is no universally accepted international consensus on oocyte morphology classification. Inter-observer and inter-laboratory variability can be substantial, leading to inconsistencies in reporting and difficulties in comparing study outcomes. This presents a significant opportunity for the development of artificial intelligence (AI)-based systems capable of evaluating morphology in an objective, consistent, and real-time manner

(Murugappan et al., 2015). The use of time-lapse imaging (TLI), which has become popular in embryo monitoring, is now being explored to analyze oocyte dynamics before and after fertilization. Early studies suggest that TLI can detect cytoplasmic movements and structural changes not visible in static assessments, providing additional indicators for evaluating oocyte viability. On the other hand, it is also important to note that maternal age plays a strong role in influencing oocyte morphology. In older women, the frequency of abnormal oocytes increases dramatically. Oocytes from women over 35 years old generally exhibit more vacuoles, central granules, and PB fragmentation. Therefore, oocyte morphology interpretation should not be separated from the clinical context of the patient, including age, infertility etiology, and the ovarian stimulation protocol used (Van Eekelen et al., 2019).

From a practical perspective, findings in this review emphasize the importance of developing standardized and evidence-based guidelines for oocyte morphology assessment. Fertility laboratories are encouraged to implement structured and documented morphology scoring and to regularly train embryologists to ensure consistent evaluations. In the future, the integration of digital technology into oocyte assessment is expected not only to enhance the accuracy of high-quality oocyte selection but also to accelerate clinical decision-making in IVF programs (Wu et al., 2022). Thus, this discussion underscores that oocyte morphology is not merely a predictive factor but also a potential indicator of oocyte health and biological readiness to support fertilization and competent embryo development. IVF success should not rely solely on final outcomes (such as clinical pregnancy), but also on optimal gamete selection from the outset, where oocyte morphology plays a central role that must not be overlooked (Meneghini et al., 2023). Although oocyte morphology has proven to provide early predictions of fertilization success and embryo development potential, further discussion reveals that this understanding cannot be separated from the underlying molecular and biochemical complexity. One important area gaining attention is the relationship between oocyte morphological phenotypes and gene expression, particularly genes involved in oocyte maturation, cell division, and energy metabolism.

Translational research has shown that morphologically normal-looking oocytes do not always possess a healthy transcriptomic or epigenetic profile. For example, oocytes with low cytoplasmic granularity and normal-looking zona pellucida may exhibit abnormal expression in mitochondrial genes or cell cycle regulators. This poses a significant challenge in the field of in vitro fertilization, as it demonstrates that morphology provides only a macroscopic view and does not necessarily reflect the cell's full functional condition. Therefore, morphology should be complemented with molecular biomarkers to improve predictive accuracy. Conversely, there are also cases where oocytes with "non-ideal" morphology still result in high quality embryos. This phenomenon supports the view that embryonic developmental plasticity can partially compensate for initial morphological limitations of the oocyte (Di Lorenzo et al., 2020). These compensatory mechanisms, involving the activation of reserve metabolic pathways and cellular stress responses, heavily depend on the oocyte's internal capacity to maintain homeostasis. In-depth studies of these mechanisms could open the door for the development of adjuvant therapies, such as coenzyme Q10 supplementation, melatonin, or in vitro growth factors, to improve the viability of oocytes with suboptimal morphology (Aaseth et al., 2021; Arenas-Jal et al., 2020).

Additionally, the impact of the IVF laboratory environment on oocyte morphology must also be critically assessed. Air quality, culture medium pH, incubator temperature, and even excessive microscope lighting can create misleading morphological artifacts. As such, the results of oocyte morphology assessments are highly dependent on standard operating procedures (SOPs) and the overall quality of laboratory management. This explains why study results between laboratories are often inconsistent, even when using similar patient populations and protocols. On the technological front, efforts to integrate AI- and machine learning-based morphology assessments are rapidly advancing. Several experimental studies have developed deep learning models capable of recognizing oocyte morphological patterns more objectively and quickly. These models not only reduce inter-observer bias but can also learn from thousands of historical datasets to identify morphology combinations most likely to result in high-quality embryos (Azarkh et al., 2023; Barnhart et al., 2002). The implementation of this technology into clinical practice is expected to revolutionize oocyte selection processes, providing higher predictive accuracy than conventional visual methods. Within the clinical framework, it is also important to address that decision-making based on oocyte morphology should take into account the patient's overall clinical context. For instance, in patients with low ovarian reserve (poor responders), discarding oocytes with abnormal morphology may not be a wise decision due to limited opportunitiesTherefore, morphology-based strategies should be flexible and individualized according to the patient's profile (Gualtieri et al., 2021).

Another issue worth considering is the ethical and psychological aspect of morphology-based oocyte selection. When patients are informed that their oocytes are considered “poor” in terms of morphology, this may lead to emotional distress and uncertainty. Clear education for patients about the limitations of morphology interpretation and the holistic prospects of IVF success is essential, so they can make rational decisions and not rely solely on a single laboratory parameter. In a global context, comparisons between studies also reveal that ethnic, lifestyle, and nutritional factors influence oocyte morphology. Therefore, approaches to oocyte morphology should not be separated from preventive and promotive approaches to overall reproductive health (Turathum et al., 2021).

CONCLUSSION

Oocyte morphology plays an important role as an early indicator in determining fertilization success and embryo quality in in vitro fertilization (IVF) programs. Various morphological parameters such as cytoplasmic homogeneity, the presence of vacuoles, polar body appearance, zona pellucida structure, perivitelline space, and cytoplasmic granularity have been shown to correlate with embryonic developmental potential. However, oocyte morphology alone cannot provide fully accurate predictions due to limitations including subjectivity in assessment, inter-individual variability, and the influence of laboratory environmental factors. Conventional visual evaluation of oocyte morphology provides an important initial contribution but still needs to be supported by other approaches, such as molecular analysis, mitochondrial function assessment, and modern technologies like time-lapse imaging and artificial intelligence. Moreover, the interpretation of oocyte morphology should not be done in isolation, but rather within the context of the patient's clinical profile, including age, ovarian condition, and infertility etiology. While oocyte morphology is not the sole determinant of IVF success, it remains an essential component in gamete selection strategies. The development of more objective, standardized, and technology-based evaluation systems is necessary to improve clinical prediction and optimize IVF outcomes. Further research using multidisciplinary approaches is strongly encouraged to integrate morphological, molecular, and clinical aspects comprehensively in order to enhance the quality and effectiveness of fertility services in the future.

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