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A Review On Embryo Grading And Imaging

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ABSTRACT

Even though in vitro fertilization (IVF) has advanced significantly over the past three decades, the treatment's effectiveness is still comparatively low. Finding the embryo with the highest chance of producing a child is the main task facing physicians and embryologists. The embryo viability assessment techniques used today only offer a rough indication of potential. Usually, multiple embryos are transferred to the uterus to increase the chances of a successful pregnancy. However, this frequently leads to multiple pregnancies (twins, triplets, etc.)(2), which are linked to a markedly increased risk of serious complications. A more precise evaluation of embryo viability would allow for the transfer of fewer embryos without adversely affecting the rates of IVF pregnancies. Numerous scoring systems based on morphological criteria have been developed to help identify viable embryos. These, however, primarily depend on a subjective visual analysis. More precise quantification of important embryonic traits and the removal of inter- and intra-observer variation are possible with automated evaluation of morphological features. In this paper, we review relevant works on embryo image analysis that could result in an automated and accurate grading of embryo quality, and we describe the primary embryo scoring systems currently in use. We highlight accomplishments, talk about upcoming difficulties, and suggest some potential avenues for further research in this area.

Keywords: in vitro fertilization, image analysis, and embryo grading.

INTRODUCTION

Many people who wish to start a family find it difficult to fulfill their dream of having a child, according to the 2023 Indian report on Assisted Reproductive Technology (ART) Success Rates. About 12% of Indian women of childbearing age have used an infertility service , and one in six couple are troublred concieving naturally one of the main techniques used to treat infertility is in vitro fertilization, or IVF Over a million IVF procedures are thought to be performed annually throughout the world . In developed nations, where IVF and related procedures now account for 1-4% of all births, utilization is especially high. Since the first successful IVF treatment thirty years ago, the procedure has undergone significant change. The treatment's effectiveness is still rather low, though, primarily because there is little chance

that a single embryo will successfully implant in the uterus and give birth. In order to increase the likelihood of success, IVF clinics typically transfer multiple embryos per cycle. The number of multiple pregnancies has skyrocketed as a result of this strategy, even though it has helped keep IVF pregnancy rates at a manageable level.

In INDIA , twins, triplets, or even more births make up more than 40% of post-IVF deliveries. Significantly higher risks of major complications are linked to high-order multiple pregnancies, like those commonly achieved through IVF(9). Preterm labor, uterine rupture, operative delivery, maternal haemorrhage, and preeclampsia are all more common in mothers of twins or triplets. By transferring fewer embryos to the mother's uterus each cycle—a single embryo transfer is the best method—multiple pregnancies can be easily avoided. Restricting the number of embryos transferred, however, has a detrimental effect on a patient's chances of getting pregnant every cycle. This is because the ability of the embryos created during a normal IVF cycle to develop into a viable pregnancy varies greatly. Therefore, it is crucial that the embryo selected for transfer in single embryo transfer (SET) cases is the one with the best chance of becoming pregnant and giving birth to a healthy child. At the moment, morphological evaluations carried out in the IVF lab are used to determine which embryo to transfer. Nevertheless, there is disagreement over the most precise technique for evaluating the quality of embryos, even though there have been many published studies on the subject. Furthermore, the available grading systems are susceptible to interobserver (and to some extent intraobserver) variance because they primarily rely on visual information that the embryologist obtains. Automated image analysis could improve the IVF procedure by bringing objectivity to the embryo selection process. However, the quality of the microscope image, variations in the embryo's morphology at different stages of development, the amount of data to be analyzed, the embryo's position and transparency, etc., can make it difficult to automatically evaluate the embryo's features. This paper reviews the published works toward automating these methods, discusses challenges and viewpoints, and provides a brief description of some of the most popular embryo grading systems.

Embryo grading systerm

Currently, a number of embryo grading schemes are in use. They depend on visual examination of the embryo's morphology and differ depending on the stage of development.(2) The most accurate grading system is still up for debate. Examples of embryo images on days 1, 2, 4 and 5 of development are displayed in Fig. (1), along with an assessment of their structures for grading.

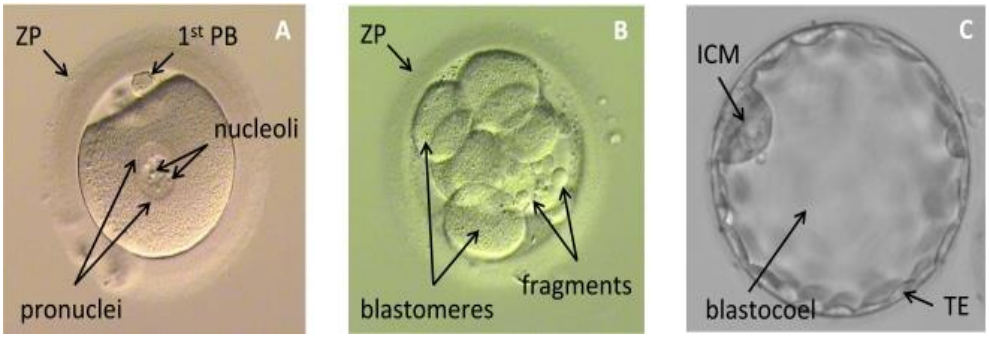

Fig.(1) *Examples of embryo image*: (*A*) *fertilised oocyte*; (*B*) *cleaving embryo*; (*C*) *blastocyst*; *ZP - zona pellucida*; 1*st PB - first polar body*; *ICM - inner cell mass*; *TE - trophectoderm*

The following are the main morphological characteristics that are important for embryo viability:

a. Cell number and degree of symmetry: an embryo has a good chance of surviving if there are an adequate number of cells and all of the cells are of a similar size.

b. Cell fragmentation: an embryo with a low percentage of cell fragments in its volume is thought to be highly viable, whereas an embryo with a large number of fragmented cells is thought to have less potential.

c. Features of the zona pellucida (ZP): the chance of a pregnancy is higher for embryos with a thinner ZP and more variation in ZP thickness.

Gardner's system for grading blastocysts

Three primary factors are taken into consideration by the widely used Gardner embryo grading system, also known as the Gardner and Schoolcraft system: expansion grade, inner cell mass (ICM) grade, and trophectoderm (TE) grade. Below is a summary of every element:

EXPANSION GRADING SYSTERM

The degree to which the embryo has developed and expanded in the culture medium is known as the expansion grade. Typically, a scale from 1 to 6 is used to evaluate it. The meaning of each grade is as follows:

Grade 1: There is no or very little expansion of the embryo.

Grade 2: The embryo's blastocoel, a tiny cavity filled with fluid, has begun to enlarge.

Grade 3: The blastocoel is bigger and the embryo has further enlarged.

Grade 4: The embryo has a large blastocoel and is even more enlarged.

Grade 5: The blastocoel has filled the majority of the embryo, causing it to expand even more.

Grade 6: With a large blastocoel and a thinning outer layer, the embryo has fully expanded.

Inner Cell Mass (ICM) Grade

The group of cells inside the embryo that will eventually give rise to the fetus is called the ICM. It is rated according to its overall quality and appearance. This is a condensed explanation of ICM grades:

Grade A: The ICM has a high density, many cells, and is closely packed.

Grade B: Although the ICM is looser or marginally less dense than Grade A, it is still regarded as being of high quality.

Grade C: A lower quality ICM is indicated by fragmentation or fewer cells.

Trophectoderm Grade

The outer layer of cells that will give rise to the placenta is called the trophectoderm. Additionally, its overall quality and appearance are used to grade it. This is a condensed explanation of TE grades:

Grade A: A cohesive layer is formed by the TE's close packing.

Grade B: The TE is still regarded as high quality even though it is a little looser or has a few small flaws.

Grade C: The TE is of lower quality because it is fragmented or contains more noticeable irregularities.

The likelihood of a successful implantation and pregnancy is generally higher for embryos with a higher TE grade. An overall evaluation of the embryo's quality and chances of successful implantation and pregnancy can be obtained by combining the expansion grade, ICM grade, and TE grade. But the embryo's grade is only one aspect of the picture. Numerous individual factors, such as your age, general fertility health, the environment in your uterus, and the doctor's skill level, affect the success of embryo transfer.

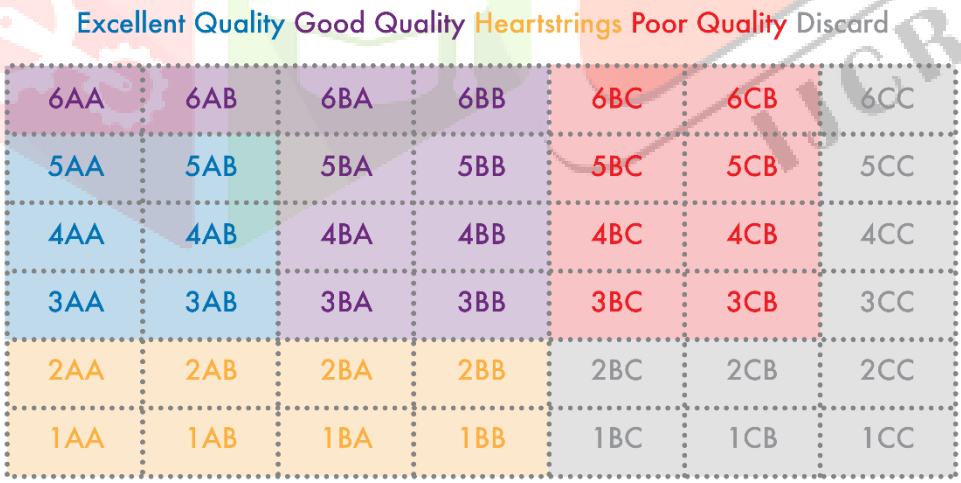

Fig. (2) *The embryo grading table to define the embryo quality*

Based on three parameters the embryo is graded as shown in Fig (2) and selected for the transfer

METHODOLOGY

The cleavage stage (Day 3) and the blastocyst stage (Day 5 or 6) are the two key developmental stages at which embryo grading usually takes place. Since the embryos have unique traits at different stages of development, different grading schemes are applied for each step.

DAY – 3 Embryo grading

Embryos are assessed on Day 3 using the following standards:

a. Cell count: By Day 3, embryos should ideally have 6–10 cells.

b. Cell size: The size and form of the cells should be comparable.

c. The term "fragmentation" describes the embryo's internal cellular waste.

A scale of 1 to 4 is frequently used to assess embryos, with assess 1 being the highest quality:

a. Grade 1: Outstanding quality with minimal fragmentation

b. Grade 2: Minimal fragmentation but good quality

c. Grade 3: Moderate fragmentation and fair quality

d. Grade 4: Severe fragmentation and poor quality

DAY – 5 Embryo grading

Embryos ought to have grown into blastocysts by Day 5. The Gardner method, which assesses three factors, is the most widely used grading scheme for blastocysts.

a. Stage of expansion (1-6)

b. Quality of Inner Cell Mass (ICM) (A, B, or C)

c. Quality of trophectoderm (TE) (A, B, or C)

A high-quality blastocyst, for instance, would receive a grade of 5AA, which denotes complete expansion with superior ICM and TE quality.

OBSERVATION

International Level

At the global scale, embryo grading methodologies exhibit considerable diversity, even though standardization efforts have been made. International guidelines, such as those developed by the Alpha Scientists in Reproductive Medicine and the Istanbul Consensus (2011), offer structured frameworks for assessing embryos at various developmental stages. Nonetheless, adoption of these guidelines varies due to differences in technological access, laboratory expertise, and healthcare policies across regions. In technologically advanced countries, the use of non-invasive imaging systems, time-lapse technology, and artificial intelligence (AI) for embryo selection is becoming increasingly common. Despite these advances, conventional morphological assessment continues to be widely practiced, often resulting in variations in grading outcomes between laboratories and clinicians.

Preimplantation genetic testing (PGT) has gained prominence internationally as an adjunct to morphological evaluation, yet its accessibility remains restricted by cost and ethical considerations. Consequently, the global consensus emphasizes the necessity for more objective and biologically relevant embryo assessment models to improve clinical reliability and outcomes.

National Level (India)

Within India, embryo grading practices display a hybrid approach, combining traditional morphological methods with emerging technological innovations. In major urban centers, leading fertility clinics have incorporated advanced tools like time-lapse incubators and AI-driven embryo selection systems. However, a large number of clinics, particularly those outside metropolitan areas, continue to depend primarily on conventional microscopic evaluation.

Variations in embryologist training, laboratory infrastructure, and economic disparities contribute to inconsistent application of grading standards across the country. Although regulatory measures, notably the Assisted Reproductive Technology (Regulation) Act, 2021, have sought to improve quality and ethical standards in ART practices, standardized protocols for embryo grading are yet to be uniformly enforced. Additionally, cultural tendencies favoring multiple embryo transfers to increase pregnancy chances can influence grading practices, occasionally contradicting the international movement towards single embryo transfer to minimize risks.

State Level (example: Chhattisgarh)

At the state level, considerable disparities are evident in embryo grading practices. In states such as chhattisgharh , where ART services are not very Well -established in many clinics But adhere closely to global standards and utilize technologies like blastocyst culture, time-lapse imaging, and genetic screening. Access to highly trained embryologists and advanced laboratory facilities in these regions supports higher consistency and precision in embryo assessment.

Conversely, clinics operating in semi-urban and rural areas often face resource limitations, which restrict the implementation of sophisticated grading techniques. Here, reliance on basic morphological observations remains common, leading to variability in embryo selection quality. The contrast between urban centers and less-developed regions within the same state underlines the need for broader access to training, infrastructure, and regulatory oversight to ensure uniformity and quality in embryo evaluation practices.

RESULT

The comprehensive review of literature on embryo grading reveals several important findings. At the international level, despite the availability of standardized guidelines, such as those proposed by the Alpha Scientists and the Istanbul Consensus, there remains considerable variation in the practical application of embryo grading systems. While advanced technologies, including time-lapse imaging and AI-driven assessment models, are increasingly being adopted in technologically advanced regions, conventional morphological evaluation continues to dominate clinical practice worldwide.

Nationally, in India, embryo grading practices show a mixed trend. Major ART centers in metropolitan areas have integrated advanced tools to enhance embryo assessment accuracy, yet a significant number of clinics still rely on traditional morphological methods due to infrastructural and economic limitations. Although regulatory frameworks like the Assisted Reproductive Technology (Regulation) Act, 2021(9), aim to bring uniformity, their influence on standardizing grading practices remains limited at present.

At the state level, a pronounced disparity is evident between urban and semi-urban/rural ART centers. States like Maharashtra have centers of excellence that align closely with international standards; however, smaller clinics often face challenges related to resources, training, and technology adoption, resulting in inconsistent embryo evaluation practices.

Overall, the findings highlight that while embryo grading remains an essential tool in ART, significant heterogeneity persists across different regions. The need for standardization, incorporation of objective technological methods, and nationwide training initiatives emerges as critical for improving the consistency and effectiveness of embryo selection, ultimately enhancing ART success rates globally and nationally.

CONCLUSION

Choosing embryos with the best chance of implantation, pregnancy, and live birth has long been made possible by embryo grading, a basic technique in the field of assisted reproductive technologies (ART). Despite their widespread use, traditional morphological assessment techniques are subjective by nature and have a low prediction accuracy. Moving beyond traditional grading methods and implementing more thorough, evidence-based procedures is obviously necessary as the need for more accurate and customized reproductive care increases. Artificial intelligence (AI), time-lapse imaging, and non-invasive metabolic and genetic profiling have all recently advanced, adding significant new dimensions to the assessment of embryos. These technologies have the ability to provide predictive analytics, objective evaluation, and ongoing monitoring that are not possible with manual grading.

In particular, AI-driven models are starting to show that they can combine intricate datasets to provide more precise forecasts of clinical outcomes and embryo viability. But before these technologies can be completely incorporated into standard clinical practice, more validation is required as their application is still in its infancy.Despite encouraging advancements, difficulties still exist. Because there is currently no widely recognized standard for embryo grading, different clinics and geographical areas have different practices. Additionally, despite the promise of developing technologies, many of them are either prohibitively expensive or require technological know-how that is not widely accessible, which raises questions around accessibility and fairness in fertility care. Additionally, ethical issues need to be taken into account, especially when it comes to the use of genetic profiling and artificial intelligence in embryo selection. The integration of multi-parameter data, including as morphology, morphokinetics, metabolomics, and genomes, into a single, objective, and clinically validated grading system is what the future of embryo grading holds. Establishing strong principles that can be embraced worldwide would require extensive, future research as well as international cooperation. In the end, improved embryo grading methods will increase overall fertility therapy safety, effectiveness, and personalization in addition to increasing conception rates. In conclusion, there is a radical change occurring in embryo grading. The sector is well-positioned to significantly improve results for people and couples seeking assisted reproduction by embracing innovation while keeping an eye on clinical value, ethical responsibility, and patient-centered care.

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