Vietnam Journal of Community Medicine, Vol. 66, English version No. 2, 42-46

# THE IMPACT OF SOME FACTORS ON OOCYTE MATURATION IN PATIENTS UNDERGOING IN VITRO FERTILIZATION AT HANOI MEDICAL UNIVERSITY HOSPITAL

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Received: 12/08/2025
Revised: 13/09/2025; Accepted: 19/12/2025

## ABSTRACT

**Objective:** To characterize oocyte maturation status and investigate clinical factors influencing oocyte maturity in controlled ovarian stimulation cycles for in vitro fertilization (IVF).

**Materials and Methods:** This retrospective descriptive study analyzed 139 IVF cycles utilizing a GnRH antagonist protocol at Center of IVF and Tissue Engineering, Hanoi Medical University Hospital, between January 2023 and June 2024. Data regarding oocyte developmental stage, ovarian stimulation parameters, and fertilization outcomes were systematically collected and evaluated.

**Results:** Mature oocytes at the metaphase II (MII) stage constituted 65.81 ± 17.92% of the total oocytes retrieved, whereas immature oocytes at the metaphase I (MI) and germinal vesicle (GV) stages accounted for 9.2 ± 11.18% and 6.88 ± 10.55%, respectively. The intracytoplasmic sperm injection (ICSI) rate was 69.36 ± 17.64%, with a corresponding fertilization rate of 88.29 ± 18.03%. Prolonged duration of infertility and lower initial doses of recombinant FSH were significantly associated with an increased proportion of immature oocytes ($p = 0,001$ and $p = 0,022$, respectively). In contrast, a longer duration of ovarian stimulation was positively correlated with higher oocyte maturation rates ($p = 0,031$). No statistically significant associations were observed between oocyte maturity and patient age, anti-Müllerian hormone (AMH) levels, body mass index (BMI), or serum concentrations of LH, estradiol, and progesterone at the time of trigger.

**Conclusion:** The degree of oocyte maturation in IVF cycles appears to be influenced by modifiable clinical variables, particularly the duration of infertility, the initial FSH dosage, and the length of ovarian stimulation. Further large-scale studies are needed to better elucidate the role of these factors for optimizing oocyte quality and enhancing clinical outcomes.

***Keywords:*** Oocyte, oocyte maturation, in vitro fertilization (IVF).

## 1. INTRODUCTION

Oocyte maturation is a pivotal determinant of the success of in vitro fertilization (IVF). This process can be assessed through multiple parameters, including morphological characteristics, chromosomal configuration, and metabolic activity, with morphological evaluation being the most widely adopted in clinical practice. A variety of factors can influence the maturation of oocytes retrieved during IVF cycles. Oocyte formation and development depend on the follicular and ovarian microenvironment, which is dynamic and subject to modulation by systemic factors such as maternal age, body mass index (BMI), etiology of infertility, and duration of infertility.

In a natural menstrual cycle, the majority of follicles undergo atresia, with only one dominant follicle selected for ovulation. In contrast, during controlled ovarian

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stimulation (COS), administration of exogenous follicle-stimulating hormone (FSH) promotes the concurrent maturation of multiple follicles, potentially altering the follicular milieu and thereby affecting the maturation process.

Previous research by Borges et al. has indicated that 10 - 30% of oocytes remain immature following retrieval [1],[2]. Clinically, oocytes at the metaphase II (MII) stage are considered optimal for fertilization because of their superior developmental competence and higher potential to yield high-quality embryos [3]. Consequently, investigating the factors that influence oocyte maturation is essential for enabling clinicians to individualize stimulation protocols, thereby improving the quality of retrieved oocytes. However, available studies – both globally and in Vietnam – remain limited, and their findings are often inconsistent.

In light of these gaps, we conducted this study with the objectives of: (1) describing the characteristics of oocyte maturation and (2) evaluating selected clinical factors associated with oocyte maturity in patients undergoing IVF at Hanoi Medical University Hospital.

## 2. MATERIALS AND METHODS

### 2.1. Study population

- Inclusion criteria:

+ IVF cycles performed at the Center of IVF and Tissue Engineering, Hanoi Medical University Hospital, between January 2023 and June 2024.

+ Controlled ovarian stimulation using a GnRH antagonist protocol.

- Exclusion criteria:

+ Oocyte donation cycles (either donor or recipient).

### 2.2. Study design

- Study type: Retrospective descriptive study.

- Sample size and sampling method: Convenience sampling was applied, including all cycles meeting the inclusion and exclusion criteria during the study period.

- Study procedure:

+ Ovarian stimulation and oocyte maturation: Ovarian stimulation commenced on day 2 of the menstrual cycle using a GnRH antagonist protocol with exogenous follicle-stimulating hormone (FSH) preparations (Follitrope, Gonal-F, Menopur, Menogon). GnRH antagonist (Cetrotide) was initiated on stimulation day 5–6. FSH administration continued until at least two follicles reached ≥18 mm in diameter. Final oocyte maturation was triggered with either human chorionic gonadotropin (hCG; IVF-C, Ovitrelle) or a GnRH agonist (Diphereline). Oocyte retrieval was performed 34–36 hours after trigger administration.

+ Oocyte morphological asessment: Retrieved oocytes were incubated in G-IVF medium for approximately 2.5 hours, followed by denudation using Hyase medium. Oocyte morphology was assessed by an experienced embryologist prior to intracytoplasmic sperm injection (ICSI), typically 38–39 hours after trigger. Oocyte maturity was classified according to the 2012 VINAGOFPA consensus on oocyte and embryo evaluation [4].

**Table 1. Assessment of oocyte maturity based on the consensus for evaluation and classification of oocytes and embryos in assisted reproduction**

| Maturity stage | Description |
|---|---|
| MII oocyte | Round oocyte with a visible first polar body (PB) in the perivitelline space (PVS). |
| MI oocyte | Absence of a germinal vesicle and absence of a first PB. |
| GV oocyte | Presence of a spherical germinal vesicle containing a prominent nucleolus. |
| Degenerated oocyte | Opaque cytoplasm with dark inclusions. |
| Abnormal oocyte | Abnormal zona pellucida (dark, irregular), abnormal PVS (narrow, wide, granular), abnormal PB morphology (fragmented, enlarged, irregular), granular cytoplasm, vacuoles, smooth endoplasmic reticulum aggregates, etc. |

+ ICSI technique: MII oocytes (with visible PB) were selected under an inverted microscope. Using a micromanipulation system, a single motile sperm was injected into the ooplasm. Injected oocytes were cultured in Continuous Single Culture® medium (FUJIFILM Irvine Scientific) at 37°C, 6% $CO_2$. Fertilization assessment was performed 16–20 hours post-ICSI.

- Variables and outcome measures

+ Patient characteristics: Age, duration of infertility, BMI, antral follicle count (AFC), serum AMH, serum LH, estradiol, and FSH on stimulation start day; serum LH, estradiol, and progesterone on trigger day; initial daily FSH dose; stimulation duration.

+ Oocyte outcomes: Total number of retrieved oocytes, proportions of MII, MI, GV, abnormal, and degenerated oocytes.

+ Fertilization outcomes: ICSI rate, fertilization rate.

### 2.3. Statistical analysis

Data were analyzed using SPSS version 26.0. Descriptive statistics were applied for baseline characteristics. Multivariate regression analysis was performed to evaluate

associations between clinical variables and oocyte maturation outcomes.

### 2.4. Ethical considerations

This retrospective study utilized data extracted from medical records without influencing patient treatment outcomes. Data collection was approved by the hospital and conducted in compliance with institutional regulations. Patient confidentiality was maintained by coding all personal identifiers.

## 3. RESULTS

A total of 139 in vitro fertilization (IVF) cycles employing controlled ovarian stimulation with a GnRH antagonist protocol were analyzed.

### 3.1. Baseline characteristics

The baseline demographic and clinical characteristics of the study population are presented in Table 2. The mean patient age was 34.57 ± 4.79 years (range, 23–47). The average duration of infertility was 2.49 ± 2.15 years, with the longest recorded duration being 13 years. The mean body mass index (BMI) was 21.26 ± 2.28 kg/m$^2$, indicating that most patients were within the normal range according to WHO classification. The mean antral follicle count (AFC) was 13.02 ± 6.34, and the mean serum anti-Müllerian hormone (AMH) concentration was 3.76 ± 3.03 ng/mL.

**Table 2. Baseline demographic and clinical characteristics of the study population**

| Characteristic | Mean ± SD | Min | Max |
|---|---|---|---|
| Age (years) | 34.57 ± 4.79 | 23 | 47 |
| Duration of infertility (years) | 2.49 ± 2.15 | 1 | 13 |
| BMI (kg/m$^2$) | 21.26 ± 2.28 | 15.63 | 30.49 |
| AFC (n) | 13.02 ± 6.34 | 3 | 60 |
| AMH (ng/mL) | 3.76 ± 3.03 | 0.5 | 23.1 |
| LH at stimulation start (mIU/mL) | 6.64 ± 6.05 | 1.77 | 62.7 |
| Estradiol on the day of ovulation induction (pg/mL) | 98.09 ± 78.11 | 11.76 | 539.87 |
| FSH at stimulation start (mIU/mL) | 6.77 ± 2.80 | 1.82 | 29.11 |
| Initial daily FSH dose (IU/day) | 294.71 ± 47.08 | 75 | 425 |
| Duration of stimulation (days) | 10.03 ± 1.03 | 7 | 13 |
| LH at trigger (mIU/mL) | 3.65 ± 3.27 | 0.10 | 20.37 |
| Estradiol at trigger (pg/mL) | 4434 ± 2945.11 | 243.1 | 18969 |
| Progesterone at trigger (ng/mL) | 2.31 ± 2.27 | 0.44 | 11.53 |

### 3.2. Oocyte characteristics and fertilization outcomes

Among all oocytes retrieved, metaphase II (MII) oocytes accounted for 65.81 ± 17.92% (mean 9.78 ± 5.85 oocytes per cycle). Immature oocytes at the metaphase I (MI) and germinal vesicle (GV) stages represented 9.20 ± 11.18% (mean 1.42 ± 2.10) and 6.88 ± 10.55% (mean 1.10 ± 1.69), respectively. Abnormal oocytes accounted for 6.96 ± 9.17%, and degenerated oocytes represented 11.39 ± 13.53%. The proportion of oocytes used for intracytoplasmic sperm injection (ICSI) was 69.36 ± 17.64% (mean 10.29 ± 5.89), with a mean fertilization rate of 88.29 ± 18.03% (Table 3).

**Table 3. Oocyte maturation status and fertilization outcomes**

| Oocyte stage / outcome | Mean ± SD | % per cycle ± SD |
|---|---|---|
| MII oocytes | 9.78 ± 5.85 | 65.81 ± 17.92% |
| MI oocytes | 1.42 ± 2.10 | 9.20 ± 11.18% |
| GV oocytes | 1.10 ± 1.69 | 6.88 ± 10.55% |
| Abnormal oocytes | 1.02 ± 1.39 | 6.96 ± 9.17% |
| Degenerated oocytes | 1.92 ± 2.58 | 11.39 ± 13.53% |
| Total oocytes retrieved | 15.23 ± 8.45 | – |
| Oocytes used for ICSI | 10.29 ± 5.89 | 69.36 ± 17.64% |
| Fertilized oocytes | 9.12 ± 5.37 | 88.29 ± 18.03% |

### 3.3. Factors associated with GV oocyte proportion

Multivariate regression analysis identified three factors significantly associated with the proportion of GV-stage oocytes: prolonged duration of infertility ($p = 0.001$, $\beta = 0.277$), lower initial daily FSH dose ($p = 0.022$, $\beta = -0.230$), and shorter duration of ovarian stimulation ($p = 0.031$, $\beta = -0.178$). The model explained 25.4% of the variance in GV oocyte

proportion ($R^2$ = 0.254). No other clinical or hormonal parameters demonstrated significant associations (Table 4).

**Table 4. Multivariate regression analysis of factors influencing GV oocyte proportion**

| Variable | GV oocyte rate | |
|---|---|---|
| | Beta | p-value |
| Age (years) | -0.200 | 0.830 |
| Duration of infertility (years) | 0.277 | 0.001* |
| BMI (kg/m$^2$) | 0.005 | 0.955 |
| AFC (n) | -1.990 | 0.057 |
| AMH (ng/mL) | 0.200 | 0.866 |
| FSH at stimulation start (mIU/mL) | -1.200 | 0.162 |
| LH at stimulation start (mIU/mL) | 0.104 | 0.236 |
| Estradiol at stimulation start (pg/mL) | -1.540 | 0.081 |
| LH at trigger (mIU/mL) | 0.089 | 0.290 |
| Estradiol at trigger (pg/mL) | -0.018 | 0.871 |
| Progesterone at trigger (ng/mL) | -0.530 | 0.528 |
| Initial daily FSH dose (IU/day) | -0.230 | 0.022* |
| Duration of stimulation (days) | -0.178 | 0.031* |

**: Significant at p < 0.05The regression model explained 25.4% of the variance in GV oocyte proportion ($R^2$ = 0.254)*

**Factors associated with MI oocyte proportion**

No statistically significant associations were observed between the proportion of MI-stage oocytes and any of the evaluated clinical or hormonal parameters (all p > 0.05). The regression model explained only 7.2% of the variance in MI oocyte proportion ($R^2$ = 0.072) (Table 5).

**Table 5. Multivariate regression analysis of factors influencing MI oocyte proportion**

| Variable | MI oocyte rate | |
|---|---|---|
| | Beta | p-value |
| Age (years) | 0.063 | 0.549 |
| Duration of infertility (years) | -0.124 | 0.177 |
| BMI (kg/m$^2$) | -1.840 | 0.050 |
| AFC (n) | 0.014 | 0.906 |
| AMH (ng/mL) | -0.350 | 0.727 |
| FSH at stimulation start (mIU/mL) | 0.046 | 0.628 |
| LH at stimulation start (mIU/mL) | 0.117 | 0.223 |
| Estradiol at stimulation start (pg/mL) | -0.132 | 0.175 |
| LH at trigger (mIU/mL) | 0.023 | 0.803 |
| Estradiol at trigger (pg/mL) | 0.026 | 0.831 |
| Progesterone at trigger (ng/mL) | -0.039 | 0.676 |
| Initial daily FSH dose (IU/day) | 0.001 | 0.995 |
| Duration of stimulation (days) | -0.450 | 0.622 |

No variable demonstrated a statistically significant association (all p > 0.05). The model explained 7.2% of the variance in MI oocyte proportion ($R^2$ = 0.072).

## 4. DISCUSSION

In the present study of 139 IVF cycles utilizing a GnRH antagonist protocol, the mean number of oocytes retrieved per cycle was 15.23 ± 8.45. Among these, mature oocytes at the MII stage constituted the majority (65.81 ± 17.92%), followed by MI-stage oocytes (9.20 ± 11.18%), GV-stage oocytes (6.88 ± 10.55%), abnormal oocytes (6.96 ± 9.17%), and degenerated oocytes (11.39 ± 13.53%). These results indicate an overall favorable ovarian response to stimulation.

The proportion of oocytes subjected to ICSI was 69.36 ± 17.64%, with a mean of 10.29 ± 5.89 oocytes per cycle. The fertilization rate was 88.29 ± 18.03%, which is comparable to the findings of Do Trong Can et al. (2023), who reported a fertilization rate of 67.92 ± 31.34% [5]. Despite these encouraging outcomes, a notable proportion of oocytes remained immature, abnormal, or degenerated, underscoring the need for further optimization of stimulation protocols to enhance oocyte quality.

A significant positive association was observed between infertility duration and the proportion of GV-stage oocytes (p = 0.001). This finding is consistent with the study by Hee Jun Lee et al. (2012), which analyzed 195 IVF cycles and reported that women over 41 years of age exhibited the highest proportion of immature oocytes (>50%) [6]. Prolonged infertility is often associated with advanced maternal age and diminished ovarian reserve, both quantitatively and qualitatively, which may impair oocyte maturation and increase the prevalence of

**GV-stage oocytes**

Multivariate regression analysis further demonstrated that a longer ovarian stimulation duration was associated with a lower proportion of GV-stage oocytes. This observation aligns with the findings of Papri Sarkar (2019), who reported the highest live birth rates among patients with a standard stimulation duration (37.3%) compared with prolonged (25%) or shortened stimulation (20.8%) [7]. Similarly, Meleen Chuang (2010) found that, among

699 IVF cycles, those resulting in live births had slightly shorter stimulation durations (11.1 vs. 11.5 days), and stimulations lasting ≥13 days were associated with reduced live birth rates compared to those lasting 10–12 days [8].

Interestingly, in our cohort, higher initial FSH doses were associated with a reduced proportion of GV-stage oocytes. In contrast, Minli Liu (2024) reported that lower initial FSH doses conferred greater benefits in terms of oocyte yield, quality, fertilization, and embryo development [9]. This discrepancy highlights the ongoing debate regarding the optimal initial FSH dose, which should be individualized based on AMH, AFC, age, and the patient's financial circumstances.

No significant associations were detected between LH concentrations on the trigger day and either oocyte maturity or fertilization rates in our study. However, Vanessa Kalinowska et al. (2024) found that higher LH levels at trigger were correlated with a reduced number of MII oocytes ($R^2$ = 0.45, p = 0.04) [10]. The divergence between these findings may be explained by the smaller sample size in our study, which could have limited the statistical power to detect such relationships.

## 5. CONCLUSION

Assessment of oocyte quality, particularly the degree of nuclear maturation, is a critical determinant of IVF success. The present study identified infertility duration, ovarian stimulation duration, and the initial FSH dose as significant factors associated with oocyte maturity. No statistically significant associations were observed with patient age, AMH levels, BMI, or pre-trigger serum concentrations of LH, estradiol, and progesterone. Further large-scale, prospective studies are warranted to better elucidate the role of these variables and to refine ovarian stimulation strategies for optimizing IVF outcomes.

## ACKNOWLEDGEMENTS AND DECLARATION OF INTERESTS

The authors gratefully acknowledge the support of the staff at the Center for Reproductive Support and Tissue Engineering, Hanoi Medical University Hospital, for facilitating the conduct of this study.

The authors declare that there are no conflicts of interest related to this work.

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