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Utilization Patterns and Clinical Outcomes Following Oocyte Cryopreservation in Turkey: A Multicenter Cohort Study Within a Nationally Regulated Setting

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ABSTRACT

Purpose: To analyse the utilization patterns, patient characteristics, and reproductive outcomes of oocyte cryopreservation (OC) performed under the current fertility preservation (FP) framework in Turkey.

Methods: This retrospective multicenter cohort study analyzed data from Ministry of Health-accredited FP programs across Turkey between 2005 and 2026. The study included women who underwent OC for approved medical indications, predominantly diminished ovarian reserve and FP before gonadotoxic treatment. Primary outcomes were oocyte utilization rates and reproductive outcomes among women who returned to use their cryopreserved oocytes. Secondary outcomes included socio-demographic profiling and cycle-level characteristics.

Results: A total of 1,582 women were included. Mean age at cryopreservation was 33.5±7.2 years. Most women underwent OC for diminished ovarian reserve (92.3%), while 7.6% underwent FP before treatment for malignant disease. Most participants were university-educated (63.9%) and employed (65.7%), with obstetrics and gynecology specialists being the primary source of awareness (53.3%). Mean anti-Müllerian hormone was 0.6±0.6 ng/mL, and a mean of 3.6±3.0 mature oocytes were cryopreserved per cycle. During the observation period, only 39 women (2.4%) returned to utilize their cryopreserved oocytes. Among thaw cycles, the clinical pregnancy rate per transfer was 15.6%, and the implantation rate was 12.7%.

Conclusion: In this large multicenter cohort, OC was predominantly performed in women with diminished ovarian reserve, resulting in relatively limited oocyte yield and low observed utilization during the available follow-up period. These findings provide real-world data on the characteristics, utilization patterns, and reproductive outcomes of FP programs in Turkey and may help inform future clinical practice and policy discussions.

Keywords: Fertility preservation, oocyte cryopreservation, restrictions, utilization rate

INTRODUCTION

In today's world, the demands of professional life often lead women to consider motherhood at later stages, when reproductive potential may already be in decline. Advancing age is inherently associated with diminished oocyte quality and quantity,[1] limiting the chances of successful conception compared to younger women. In this context, preserving fertility emerges as a critical consideration in life planning for many individuals. The term "fertility preservation" (FP) relates to offering women and men the opportunity to extend their reproductive potential beyond limits imposed or expected because of medical or non-medical reasons. Due to enhanced access to information and growing patient awareness, FP has become a pivotal strategy in modern reproductive medicine.

One of the most significant milestones in this field was the introduction of vitrification techniques in in virto fertilization

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(IVF) laboratories. Since the first live birth following human oocyte vitrification was reported in 1999,[2] the clinical use of this method has expanded considerably. The growing body of experience, coupled with evidence showing no increase in congenital anomaly risk in subsequent pregnancies, has led to a rise in the number of autologous oocyte cryopreservation (OC) cycles performed over the past decades.[3,4] This growing confidence has also contributed to the development of donor programs and banking strategies, further enhancing the clinical utility of oocyte vitrification.[5]

Autologous OC is currently performed for both medical and non-medical indications. Medical indications primarily include FP before potentially gonadotoxic treatments, whereas non-medical (elective) OC is generally pursued because of anticipated age-related fertility decline, reproductive life planning, or the absence of a suitable reproductive partner. In both settings, age at the time of oocyte retrieval remains one of the most important determinants of future reproductive success.[6] However, access to this technology remains uneven globally, often shaped by national legislation and cultural norms.[6-14] In Turkey, OC is regulated by the ministry of health and is currently permitted under specific medical indications. These include FP before potentially gonadotoxic treatments, as well as selected circumstances related to ovarian reserve assessment and reproductive risk. Elective OC for non-medical reasons is not currently permitted within the existing regulatory framework. The regulatory framework governing OC differs substantially across countries and may influence patient access, referral pathways, and utilization patterns. Understanding how FP programs function within different regulatory environments is therefore important for clinicians, patients, and healthcare policymakers.

Although OC has become increasingly established worldwide, relatively limited data are available regarding utilization patterns and long-term outcomes of FP programs operating under different regulatory frameworks. Thus, the aim of this multicenter cohort study was to describe patient characteristics, utilization patterns, and reproductive outcomes following OC in Turkey and to provide real-world data from a large multicenter cohort operating within a nationally regulated FP framework.

METHODS

Study Design and Setting

This retrospective multicenter cohort study was conducted at six FP programs licensed by the Turkish Ministry of Health for assisted reproductive technologies, located across different regions of Turkey. Participating centers included Kocaeli University IVF Center, Bursa Eurofertil IVF Center, Istanbul Momart IVF Center, Yüzyıl Hospital IVF Center, Bursa Pembe Mavi IVF Center, and collaborating private FP clinics. Variation in patient volume across centres reflects differences in programme size and duration rather than methodological inconsistency. Of note, the study does not compare outcomes between centres so this heterogeneity does not introduce analytical bias. Centres were recruited on the basis of voluntary participation, encompassing university-affiliated, public hospital-based, and private FP programmes across different regions of Turkey. Clinical data encompassing OC cycles performed between 2005 and 2026 were retrospectively collected from each center in anonymized form.

The primary aim of this study was descriptive: to characterise the patient profile, indications, stimulation outcomes, and utilization patterns of OC within a nationally regulated setting. The limited number of reproductive events observed during the follow-up period precluded multivariable modelling of predictors of reproductive outcomes. This represents an important direction for future prospective research in Turkey.

Study Population

Eligible participants were women who underwent OC at one of the participating centers during the study period and for whom complete clinical and laboratory records were available. Women were excluded if the cryopreservation cycle was cancelled before oocyte retrieval, if embryo cryopreservation rather than OC had been performed, or if essential clinical information was unavailable.

Data Collection

Standardized case report forms were used to extract demographic, clinical, and laboratory parameters from the electronic medical records of each center. Collected variables included age at first oocyte retrieval, body mass index (BMI), tobacco use, obstetric history, educational and occupational status, and indication for OC. Oncological status and treatment details were recorded where applicable. Ovarian stimulation data included the type and total dose of gonadotropins administered, stimulation protocol, trigger method for final oocyte maturation, and the use of adjuvant oral agents. Hormonal and ultrasound parameters included baseline serum follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), anti-Müllerian hormone (AMH), and antral follicle count (AFC). However, as serum FSH, LH, and E2 values were not uniformly documented across all participating centres and time periods and there would have been methodological and potentially normative range differences, these were not included in the primary results due to an insufficient completeness rate for meaningful summary reporting.

Oocyte retrieval outcomes comprised the total number of oocytes retrieved, the number of germinal vesicle and degenerated oocytes, the number of mature (MII) oocytes, vitrification method, storage location, and total duration of cryopreservation.

Outcomes

The primary outcome was the oocyte utilization rate, defined as the proportion of women who returned to use their cryopreserved oocytes during the observation period. Secondary outcomes included reproductive outcomes following thaw cycles (clinical pregnancy rate per transfer and implantation rate), demographic and socioeconomic characteristics, indications for OC, ovarian stimulation parameters, and oocyte yield per retrieval cycle.

Ethics Approval

This study was approved by the Kocaeli University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (approval no: KÜ GOKAEK-2025/17/18, date: 19.08.2025). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Due to the retrospective nature of the study, the requirement for written informed consent was waived in accordance with national ethical guidelines. For patients younger than 18 years of age, all procedures were performed in accordance with national regulations governing FP in minors.

Statistical Analysis

Descriptive statistics were reported as means ± standard deviation (SD) or medians with minimum-maximum (min-max) values for continuous variables, and as frequencies with percentages for categorical variables. Between-group comparisons were performed using Student's t-test or the Mann-Whitney U test for continuous variables, and the chi-square or Fisher's exact test for categorical variables, as appropriate. Statistical significance was set at $p<0.05$. All analyses were performed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA).

As this study enrolled all eligible patients from the participating centres during the study period no sample size calculation or power analysis was performed.

RESULTS

A total of 1,582 women underwent OC during the study period. The number of patients contributing data per centre was: Kocaeli University IVF Centre (n=710), Bursa Eurofertil IVF Centre (n=75), Istanbul Momart IVF Centre (n=84), Yüzyıl Hospital IVF Centre (n=75), Bursa Pembe Mavi IVF Centre (n=37), and four collaborating consultant centres (n=601). The mean age was 33.5±7.2 years (range: 14-50), and the mean BMI was 22.3±4.8 kg/m^2. Most cases (92.3%, n=1,461) were indicated for diminished ovarian reserve, while 7.6% (n=121) underwent FP following a diagnosis of malignant disease. Only seven women (0.4%) had a living child at the time of cryopreservation. Sixteen patients were aged 45 years or older, while 11 (0.7%) patients were under 18 years of age (range: 14-17 years), all of whom had been diagnosed with hematological or solid malignancies including leukemia, lymphoma, or sarcoma. Demographic characteristics and patient referral patterns are summarized in Table 1.

The majority of patients were university graduates (63.9%) and were employed (65.7%). Awareness of OC was most commonly attributed to an obstetrics and gynecology (ObGyn) specialist (53.3%), followed by media and internet sources (20.1%) and family or friends (18.2%). The remaining patients were referred by physicians other than ObGyn (8.2%), including oncologists, family practitioners, radiologists, general surgeons, pediatricians, and geneticists (Table 1).

Regarding ovarian stimulation, the antagonist protocol was used in 94.8% of cycles, while progesterone-primed and long agonist protocols were employed in 4.2% and 0.8% of cases, respectively. Random start cycles accounted for 2.7% of all stimulations. Letrozole and clomiphene citrate were co-administered with gonadotropins in 9.0% and 3.2% of cycles, respectively.

Oocyte retrieval was performed by transvaginal ultrasound guidance in 91.0% of cases, with transabdominal and laparoscopic approaches used in 4.8% and 4.1%, respectively. Mean AMH was 0.6±0.6 ng/mL and mean AFC was 5.5±3, consistent with the predominantly diminished ovarian reserve population. Mean stimulation duration was 9.9±1.4 days with a total gonadotropin dose of 3,252±992 IU. A mean of 4.5±4.0 oocytes were retrieved per cycle, of which 3.7±3.2 were mature (MII) and 3.6±3.0 were successfully cryopreserved. The ovarian hyperstimulation syndrome rate was 0.5%. Cycle characteristics, stimulation protocols, and oocyte yield are detailed in Table 2.

The mean duration of oocyte storage was 34.7±19.3 months (range: 1-101 months). A total of 137 women (8.6%) obtained ministry of health approval to extend storage beyond the legally mandated five-year limit. Among the 51 women whose cryopreservation was discontinued prior to utilization, reasons included cancer-related death (n=11), spontaneous conception (n=14), cancer recurrence or persistence precluding further treatment (n=12), and reaching the legal storage limit without wishing to extend (n=14).

Table 1. Demographic variables and patient awareness in oocyte cryopreservation patients

Variable	Number of patients (n=1582)
Age, years	33.5±7.2 (14-50)
BMI, kg/m^2	22.3±4.8 (13-47.9)
Tobacco use	311 (19.6%)
Children alive	7 (0.4%)
Education	
Secondary school	249 (15.7%)
High school	322 (20.3%)
University	1011 (63.9%)
Working status	
Employed	1040 (65.7%)
Unemployed	542 (34.2%)
Patient referral and awareness	
Obstetrics and gynecology specialist	844 (53.3%)
*Other doctors	131 (8.2%)
Family or friends	289 (18.2%)
Media-internet	318 (20.1%)
Indication for oocyte cryopreservation	
Low ovarian reserve	1461 (92.3%)
Fertility preservation after diagnosis of malignant tumors	121 (7.6%)

*Other doctors include oncologist, family practitioner, radiologist, general surgeon, pediatrician, geneticists
The data is presented as numbers and percentages or mean ± standard deviation of the mean and minimum-maximum values
BMI: Body mass index

During the study period, 39 women (2.4%) returned to utilize their cryopreserved oocytes. Of these, 27 (69.2%) had originally undergone OC because of diminished ovarian reserve and 12 (30.8%) for FP before cancer treatment. A mean of 3.3±2.8 mature oocytes were thawed per cycle. The wide SD observed for the fertilisation rate (84±42%) reflects genuine inter-cycle variability inherent to the small thaw cohort (n=39), in which cycles with a single or two oocytes thawed disproportionately influence summary statistics; no data-entry errors were identified upon re-verification of the source data.

Embryo transfer was performed in 32 of 39 thaw cycles (82.0%). A total of six pregnancies were achieved, including one biochemical pregnancy and five clinical pregnancies. The overall pregnancy rate per transfer was 18.7% (6/32), while the clinical pregnancy rate per transfer was 15.6% (5/32). The implantation rate was 12.7% (6/47 transferred embryos). Thaw cycle outcomes and reproductive results are presented in Table 3.

DISCUSSION

In this large multicenter cohort study, we evaluated utilization patterns and reproductive outcomes following OC in the setting of nationally regulated FP. Three principal findings emerged from our analysis. First, more than 90% of women undergoing OC had diminished ovarian reserve rather than oncological indications. Second, the cohort demonstrated a relatively low oocyte yield, consistent with the biological characteristics of the study population. Third, only a small proportion of women returned to use their cryopreserved oocytes during the statutory 5-year follow-up period. Collectively, these findings describe OC practice within a nationally regulated setting and highlight the importance of patient selection when interpreting utilization and reproductive outcomes.

While numerous studies have investigated FP outcomes, many have been limited by small sample sizes and short follow-up durations. However, recent studies with longer follow-up periods are beginning to provide more meaningful insights into clinical outcomes.[15,16] Against this background, our multicenter findings may contribute valuable insight into the current status of FP in Turkey and allow for comparison with international cohorts. Previous studies have reported substantial variability in utilization rates following OC, reflecting differences in patient populations, indications, follow-up duration, healthcare systems, and regulatory environments.[15-17] Consequently, utilization rates should be interpreted within the context of the characteristics of the population being studied. In our cohort, only 39 women (2.4%) returned to use their cryopreserved oocytes during the observation period. However, utilization rates require careful contextualisation, as there is no universally accepted follow-up duration for defining non-utilization after OC. Some women may return within a short period after storage, whereas others may not return for many years. Therefore, the utilization rate reported in the present study reflects observed utilization during the available follow-up period rather than the final cumulative utilization rate of the cohort. The mean storage duration of 34.7 months, with some patients exceeding eight years of storage, nevertheless provides valuable insight into real-world utilization patterns within a large multicenter cohort.

Table 2. Cycle characteristics, protocols and oocyte yield of oocyte cryopreservation cases

	Participants (n=1582)
Induction protocol	
Long agonist	14 (0.8%)
Antagonist cycle	1501 (94.8%)
Progesterone primed	67 (4.2%)
Random start	43 (2.7%)
Oral agents used with gonadotropins	
Clomiphene	52 (3.2%)
Letrozole	143 (9%)
Oocyte retrieval method	
Transvaginal ultrasound guided	1440 (91%)
Transabdominal ultrasound guided	77 (4.8%)
Laparoscopic	65 (4.1%)
AMH (ng/mL)	0.6±0.6 (0-5)
AFC	5.5±3 (1-19)
Stimulation duration (days)	9.9±1.4 (5-20)
Total gonadotropin dose (IU)	3252±992 (600-9000)
Retrieved total oocytes	4.5±4 (1-49)
Mature (metaphase II) oocytes (MII)	3.7±3.2 (1-26)
Cryopreserved oocytes	3.6±3.0 (1-26)
Ovarian hyperstimulation syndrome	9 (0.5)

The data is presented as numbers and percentages or mean ± standard deviation of the mean and minimum-maximum values
AMH: Anti-Müllerian hormone, AFC: Antral follicle count

Table 3. Cycles for reuse of oocyte cryopreservation cases

Variable	**Thaw cycles of the ocyte crypreserved cases (n=39)**
Number of M^2 oocytes thawed	3.3±2.8
*Fertilization rate (%)	84±42%
Embryo Transfer	32/39 (82%)
Day 3	23/32 (71.8%)
Day 5	9/32 (28.1%)
Embryo transfer Single	17/32 (53.1%)
Double	15/32 (46.8%)
Total number of embryos transferred (n)	47
Pregnancy rate per transfer (%)	6/32 (18.7%)
Biochemical pregnancy per transfer (%)	1/32 (3.1%)
Clinical pregnancy rate per transfer (%)	5/32 (15.6%)
Implantation rate (%)	6/47 (12.7%)

A total of 39 (2.4%) cases returned for the use of oocyte cryopreserved oocytes. Twelve of these were cryopreserved for oncological treatments and 27 of them were cryopreserved for low ovarian reserve
*Fertilization rate was calculated on a per-cycle basis

Some of these women may have conceived spontaneously and therefore no longer needed their frozen oocytes. Others may have experienced delays in marriage or encountered ambivalence, either personally or from their partners, about pursuing parenthood later in life. Understanding the reasons beyond non-utilization from a sociodemographic perspective could offer valuable guidance for improving program design and implementation.

The demographic profile of women enrolled in our program also warrants discussion. The predominance of university graduates (63.9%) and employed women (65.7%) among applicants suggests that awareness of and access to OC remains concentrated among more educated and economically independent segments of society. The predominance of university graduates and employed women may suggest disparities in awareness, access, or utilization of FP services across different socio-economic groups.

The striking imbalance in indications, with 92.3% of cases driven by diminished ovarian reserve and only 7.6% by oncological reasons, alongside the finding that non-ObGyn physicians accounted for fewer referrals than media or personal networks, suggests a systemic gap in interdisciplinary awareness. Oncologists, surgeons, and other specialists who routinely encounter women of reproductive age facing potentially gonadotoxic treatment represent an underutilised referral source, and targeted awareness initiatives could meaningfully address this deficit.

Maternal age at the time of oocyte retrieval remains one of the most important determinants of future reproductive success following OC. Previous studies have consistently demonstrated superior reproductive outcomes when oocytes are cryopreserved at younger ages.[17-19] In the present cohort, the clinical pregnancy rate per transfer was 15.6% and the implantation rate was 12.7%. These outcomes should be interpreted in the context of the study population, which was characterized by low AMH levels, low AFC values, and a limited number of cryopreserved oocytes per cycle. Collectively, these findings suggest that baseline ovarian characteristics and oocyte yield are important considerations when evaluating reproductive outcomes after OC.

International approaches to FP reveal a stark contrast between many western nations and countries with stricter regulations. In the United States, Spain, Canada, Belgium, Brazil, Australia, and Israel, elective egg freezing is liberally permitted for all adult women regardless of marital status or age, reflecting a progressive stance on reproductive autonomy.[7-10,20] The United Kingdom also has permissive policies, allowing access without age or relationship restrictions.[11] France even offers partial public funding,[7] while countries like Austria and China maintain significant restrictions, limiting access to only medical indications or married women.[12]

In Muslim-majority countries, policies on elective OC vary considerably, shaped by cultural, legal, and religious frameworks. While some nations have recently moved toward more permissive regulations, others continue to impose strict limitations. Among Islamic scholars, the procedure is broadly regarded as makruh-permissible but discouraged-which continues to influence both policy and individual decision-making across these settings.[13,14]

The findings of this study should be interpreted in the context of the patient population studied. Unlike many published elective OC cohorts, 92% of women in the present study presented with diminished ovarian reserve, which is likely to have influenced oocyte yield, utilisation patterns, and reproductive outcomes, independent of healthcare system and regulatory factors.[7-14,20] Furthermore, the relatively low AMH levels, low AFC values, and limited number of cryopreserved oocytes observed in our cohort are consistent with the characteristics of women presenting with diminished ovarian reserve. Therefore, direct comparisons with elective OC cohorts from unrestricted settings are of limited validity, given the substantial differences in indication, ovarian reserve status, and reproductive prognosis between these populations.[6,17]

Future studies focusing on referral pathways, access patterns, patient decision-making, and long-term utilization outcomes may further clarify how different healthcare systems and regulatory environments influence FP practice and outcomes across diverse patient populations.

Study Limitations

This study has several limitations that should be considered when interpreting the findings. First, the retrospective design may be associated with selection bias and incomplete data capture despite the use of standardized data collection procedures across participating centers. Second, the study period spans 21 years (2005-2026), during which substantial advances occurred in vitrification technology, ovarian stimulation protocols, laboratory practices, and regulatory policy in Turkey. These changes may have influenced oocyte yield, cryopreservation efficiency, and utilisation patterns in a non-uniform manner across the cohort. However, as year-of-procedure data were not uniformly available across all participating centres, temporal subgroup analyses could not be performed, and the overall results should therefore be interpreted as reflecting aggregate practice across the entire study period rather than current clinical standards. Third, utilization rates should be interpreted as observed utilization during the available follow-up period rather than ultimate lifetime utilization rates. Women may return to use their cryopreserved oocytes after highly variable storage durations, and no universally accepted follow-up threshold exists for defining non-utilization. Fourth, only a limited number of women returned to utilize their cryopreserved oocytes, resulting in a relatively small number of thaw cycles and reproductive events. Consequently, reproductive outcome estimates should be interpreted cautiously. Detailed post-warming oocyte survival data were not uniformly available across participating centers and therefore could not be analyzed.

Although two indication groups were identifiable, a formal subgroup comparison was not performed, as the oncological group was numerically small (n=121), clinically heterogeneous across centres, and the limited reproductive events precluded meaningful statistical comparison. Finally, complete follow-up data on live births, pregnancy loss, ectopic pregnancy,

and obstetric outcomes were not uniformly available across participating centres. This represents a significant limitation, as live birth rate per transfer, rather than clinical pregnancy rate, is the most clinically meaningful endpoint in assisted reproduction. Future studies with prospective follow-up and standardized outcome reporting are strongly encouraged to address this gap.

The present study also has several important strengths. To the best of our knowledge, it represents one of the largest multicenter cohorts evaluating OC practice in Turkey. The inclusion of 1,582 women from multiple FP programs provides a comprehensive overview of patient characteristics, indications, stimulation outcomes, and observed utilization patterns within a real-world clinical setting. In addition, the study includes both women undergoing FP before potentially gonadotoxic treatment and women undergoing OC because of diminished ovarian reserve, thereby reflecting the spectrum of patients currently accessing these services in routine clinical practice in Turkey. Finally, the availability of follow-up data extending beyond eight years in some patients provides valuable insight into long-term utilization behavior following OC.

CONCLUSION

In this large multicenter cohort, OCin Turkey was performed predominantly in women with diminished ovarian reserve, resulting in relatively limited oocyte yield and low observed utilization during the available follow-up period. The reproductive outcomes observed among women who returned to use their cryopreserved oocytes should be interpreted in the context of the underlying ovarian reserve characteristics of the study population and the limited number of thaw cycles.

This large multicenter cohort provides insight into patient characteristics, utilisation patterns, and reproductive outcomes following OC in a regulated FP setting. The predominance of women presenting with diminished ovarian reserve highlights the potential importance of timely FP counseling, improved public awareness, and effective interdisciplinary referral pathways when designing future FP strategies. Future prospective studies in Turkey with longer follow-up and complete live birth reporting are needed to better define long-term utilization behavior and the ultimate effectiveness of this nationally regulated FP program.

Ethics

Ethics Committee Approval: This study was approved by the Kocaeli University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (approval no: KÜ GOKAEK-2025/17/18, date: 19.08.2025).

Informed Consent: Not applicable. The manuscript does not contain any individual person's data in any form (including individual details, images, or videos). Due to the retrospective nature of the study and the use of anonymized data, the requirement for informed consent to participate was waived by the Non-Interventional Clinical Research Ethics Committee of Kocaeli University Faculty of Medicine.

Authorship Contributions

Surgical and Medical Practices: G.A., A.İ.T., H.U.Ş., S.S., E.D., Concept: G.A., Design: G.A., Data Collection or Processing: G.A., A.İ.T., H.U.Ş., S.S., E.D., Analysis or Interpretation: G.A., Literature Search: G.A., Writing: G.A.

Footnotes

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