

# Demographic distributions and clinical results of assisted reproduction techniques in Turkey in 2019: a descriptive survey

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## Abstract

**Objective:** The aim of this study was to describe characteristics and outcomes of assisted reproductive technology (ART) cycles performed in 2019 in Turkey.

**Material and Methods:** One-hundred and sixty-five ART centers in Turkey were invited to submit data. The survey was sent to center directors via e-mail with anonymous links by Qualtrics™. The survey involved questions about their patient characteristics, clinical practices, and outcomes.

**Results:** Forty-one (24.8%) centers responded to e-mails, and data gathered from 25 centers was included in the analyses. In 25 centers, 18,127 fresh or frozen transfers were carried out during the study period, of which 7796 (43.0%) were fresh and the rest were either frozen (45.2%) or embryo transfers (ET) with preimplantation genetic testing (PGT) (11.8%). The live birth rate per ET was as 30.6%, 40.1%, and 50.7% in fresh, frozen and PGT cycles, respectively. A single embryo was transferred in 65.3% of all transfers and singleton live births comprised 86.1% of all deliveries. For cycles with intrauterine insemination, 1407 were started in 2019, and 195 clinical pregnancies, 150 live births with 19 multiple pregnancies occurred. A total of 1513 ART cycles were initiated for foreign patients. Russia (29.6%), Germany (7.4%), Iraq (4.6%), Uzbekistan (3.1%), and Syria (1.4%) were the top five countries with most patients coming to Turkey for ART.

**Conclusion:** The survey results are in parallel with the reports of international institutions and organizations. With repeated editions, the data collected with annual surveys can be used to inform ART practices in the coming years. (J Turk Ger Gynecol Assoc 2024; 25: 18-23)

**Keywords:** Assisted reproduction technology, medically assisted reproduction, in-vitro fertilization, embryo transfer

## Introduction

Assisted reproductive technology (ART) is a widely used and highly effective treatment for infertility. However, a comprehensive national registry is required to audit ART outcomes properly. The absence of publicly available national data concerns patients, providers, and researchers and is needed to understand the success rates and safety of ART practice in any jurisdiction.

Annual reports on ART help provide reliable and aggregated data to inform healthcare policies, enable calculation of associated costs, facilitate the development of and access to treatment and increase the quality of care provided. Among such national and international registries are the ones managed by the Centers for Disease Control and Prevention and Society for Assisted Reproductive Technology (SART)/American Society of Reproductive Medicine in the USA, by the Human Fertilization and Embryology Authority (HEFA) in the UK and by European Society of Human Reproduction and Embryology (ESHRE) in the Europe an Community (1-3).

Information provided by these registries contributes to significant improvements in ART practice. A noteworthy example is limiting the number of embryos transferred. The common practice of multiple embryo transfers (ET) and advances in embryology laboratory procedures in the 1990s resulted in an increased incidence of multiple pregnancies. As a result, ART pregnancies were associated with increased maternal/antenatal morbidity. Increased awareness provided by the registries prompted mandatory, as well as voluntary, decreases in the number of embryos transferred.

Continuous effort is required to optimize data collection in order to enhance surveillance and quality assessment in ART. Standardized annual reports would help identify areas for improvement. In addition, transparency of national ART

statistics may help international patients seeking treatment in a particular country.

The aim of the current multicenter, descriptive survey was to describe demographic distributions and clinical results of ART cycles in Turkey in 2019 through aggregated, anonymized data.

## Material and Methods

An invitation e-mail (Supplement 1) was sent to clinic directors in public and private ART centers. The mailing list was created by combining the shared communication lists of non-profit associations operating in our country, such as the Turkish Reproductive Health and Infertility Association (TSRM), the Clinical Embryology Association and the In-Vitro Fertilization (IVF) Centers Association. If a center did not respond within a week, a repeat e-mail was sent. For those centers with telephone number information, a reminder call was placed. Data were collected in an anonymized manner at both clinic and individual patient level.

The questionnaire followed the template of the ESHRE [European IVF Monitoring (EIM)] consortium. It included an online informed consent form for the clinic directors, with an invitation statement from the survey's principal investigator, and a brief explanation of the purpose. It was stressed that participation was voluntary and that the responses would remain anonymous. The survey inquired about data for the year 2019.

The survey was prepared with Qualtrics™, an internet-based commercial survey system. The survey consisted of 12 question blocks, including preliminary information with 25 questions (Supplement 2). The survey was designed using a set of validated benchmarks in line with the training videos suggested by Qualtrics™. Artificial intelligence-assisted adaptive inquiry methods created by Qualtrics™ were used to lessen the question counts and, where applicable, the complexity

of the items. To prevent multiple data submissions by the same participant, Qualtrics™ places a cookie in participants' browsers when they submit a response. All security measures offered to the Qualtrics™ users can be accessed from the links in supplementary files. Qualtrics™ is ISO 27001, 27017, and 27018 certified and is a FedRamp (US government security compliance standard with over 300 audits based on the highly respected NIST 800-53 that requires ongoing monitoring and periodic independent reviews) (4).

The projected study duration was 60 days, with estimations of 15 days for volunteers to fill out the survey, 10 days for data collection and analysis, five days to apply the preliminary analysis and share the initial report with the participants, and 30 days to perform the final analysis and compose the manuscript.

### Definition of terms used in the survey

The parameters for documenting ART treatment outcomes were defined as the standards set by World Health Organization/International Committee for Monitoring Assisted Reproductive Technologies (WHO/ICMART). To illustrate, clinical pregnancy is defined as ultrasonographic confirmation of one or more gestational sacs or definitive clinical signs of pregnancy, while delivery is defined as live and/or stillbirth occurring after the 22<sup>nd</sup> gestational week. The live birth rate (LBR) per ET was defined as the ratio of ETs to the number of births, irrespective of the number of babies born or the number of embryos transferred. Preterm delivery was defined as births before 37 weeks of gestation, late preterm as births between 32 and 37 weeks and very preterm deliveries as births before 32 weeks of gestation. All the terms were based on WHO/ICMART definition and explained above in the appropriate question blocks in the survey (5). Ovarian hyperstimulation syndrome (OHSS) was defined and staged according to the Practice Committee of the American Society for Reproductive Medicine guideline on OHSS in 2016 (6).

The study was approved by the Koç University Ethics Committee (approval number: 2022.386.IRB1.141, date: 07.11.2022). The authors confirm that fully informed, freely given and written consent to participate were obtained from all participants (cohort) in the present study.

### Statistical analysis

As this was a descriptive study, only measures of frequency (count, percent, and frequency) were used, and no comparative statistical analyses were conducted.

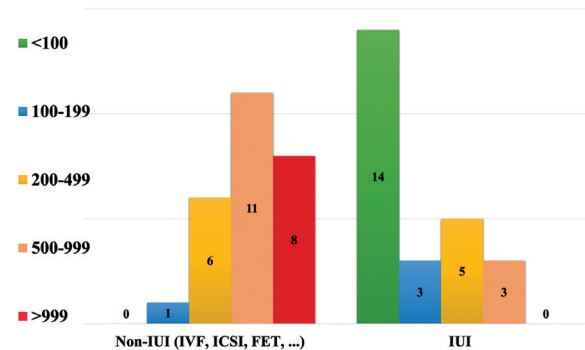
## Results

The survey was sent to the directors of 165 ART centers via e-mail with anonymous links provided by Qualtrics™. Of these,

41 (24.8%) replied and 26 (15.76%) completed the questionnaire. Data from 25 (15.15%) centers that answered more than 50% of the questions were included in the report. Figure 1 shows annual ART cycles carried out during the study period.

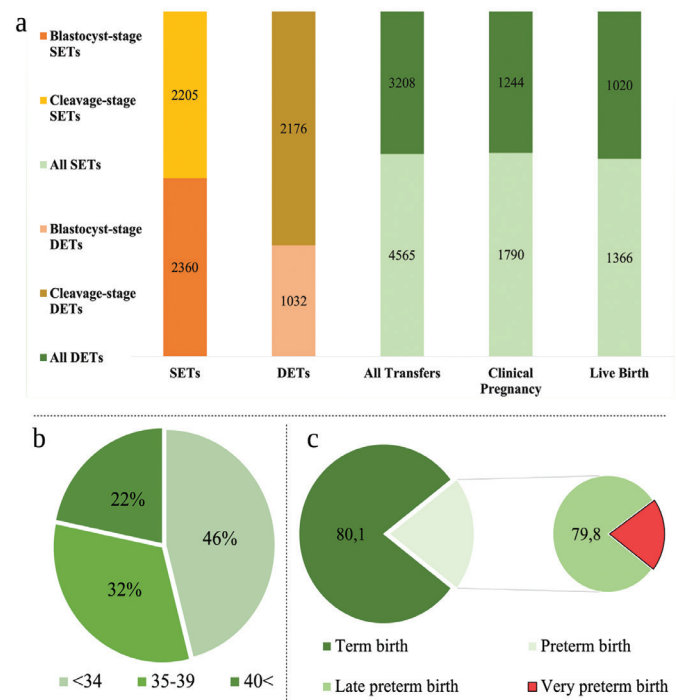
### Overall results per ART cycle

The results based on the stage (cleavage, blastocyst) or the number of the transferred embryos in the fresh or frozen cycles and the distribution according to the patient's age at oocyte-pickup and gestational age at delivery are shown in Figure 2, Figure 3a-c), respectively. Additional characteristics of the (a)



**Figure 1. Distribution of clinics by the number of cycles they performed in 2019**

**IUI: Intrauterine insemination, IVF: In-vitro fertilization, ICSI: Intracytoplasmic sperm injection, FET: Frozen-embryo transfer**



**Figure 2. Distributions and clinical outcomes by (a) transferred embryo number/stage, (b) age and (c) birth week in fresh cycles**

**SET: Single embryo transfer, DET: Double embryo transfer**

fresh, (b) frozen or (c) preimplantation genetic test (PGT) transfers are presented in Figure 4.

**Intrauterine insemination**

A total of 1407 intrauterine insemination (IUI) procedures were performed in 25 centers in 2019. Women were younger than 35 years in 80.9%, between 35 and 39 years old in 16.3% and 40 years or older in 2.8% of cycles. Of these, 195 cycles (13.8%) resulted in clinical pregnancy, and 150 (10.6%) resulted in delivery. Of all births, 15 resulted in twin pregnancies and four

were higher order. Pregnancy outcomes were not available for six cycles.

**Fresh cycles**

In the 25 clinics included in the survey data, 11,121 oocyte pick-ups (OPU) were conducted, and following IVF or intracytoplasmic sperm injection (ICSI), 7796 fresh ET procedures were performed. In 2696 cycles, sperms were obtained by surgical procedures [testicular sperm extraction (TESE), micro-TESE, or fine needle aspiration]. A single embryo was transferred in 4565 (58.5%) fresh transfers, and in 3208, double embryos were transferred. Data for 23 transfers were missing. Of all fresh transfers, 626 resulted in pregnancy loss, 3036 (38.9%) resulted in clinical pregnancy, 2388 (30.6%) ended in a live birth, 279 of which were twin or higher-order pregnancies. Pregnancy outcomes of 22 cycles were missing.

**Frozen cycles**

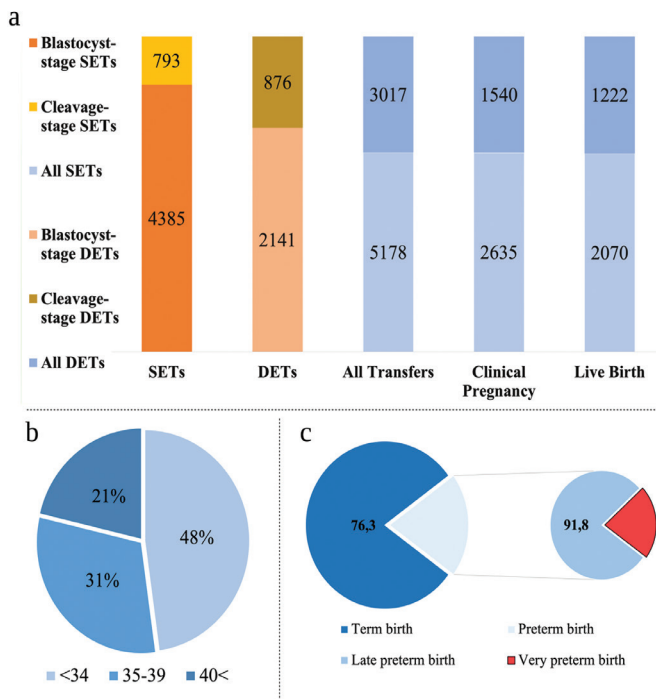
These consisted of 8433 thawings and 8197 transfers were performed, of which 5178 (63.1%) were single ETs. Data for two transfers were missing. Among all frozen cycles, 811 resulted in pregnancy loss, 4177 (50.9%) resulted in clinical pregnancy, and 3294 (40.1%) in a live birth, 449 of which were twin or higher-order pregnancies. Pregnancy outcomes of 72 cycles were missing.

**Cycles with PGT**

In the survey, information was not requested about the platform used for genetic analysis in the PGT procedure (comparative genomic hybridization, single-nucleotide polymorphism, next-generation sequencing arrays) or on the reported result of PGT, for example whether mosaicism was reported, or which embryos were transferred in the presence of mosaicism. Therefore, the results should be interpreted cautiously in the absence of these details. Nevertheless, according to the data from the 25 centers, 1252 (58.6%) clinical pregnancies after 2134 ETs were achieved, of which 1083 (50.7%) resulted in a live birth. In addition, 130 women experienced pregnancy loss, and pregnancy outcomes of 39 cycles were missing.

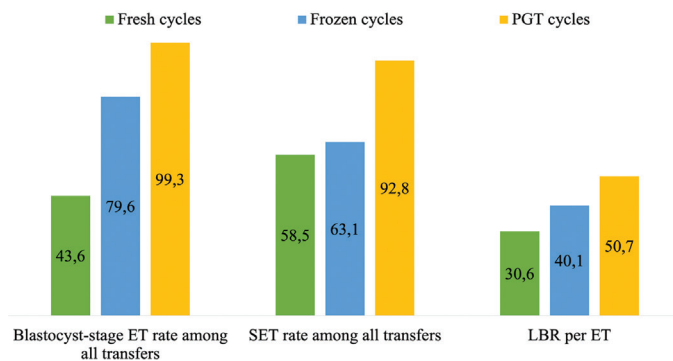
**Complications during ART applications and fetal reduction procedures**

Seventy-three women were reported to require hospitalization for stage 3 or above OHSS. Data for complications due to OPU procedures that resulted in hospitalization were also collected. Moreover, 55 women were hospitalized due to bleeding, eight because of infection and two for other causes. None of these resulted in death. A total of 15 fetal reduction procedures were performed in the 25 centers in 2019.



**Figure 3. Distributions and clinical outcomes by (a) transferred embryo number/stage, (b) age and (c) birth week in frozen cycles**

SET: Single embryo transfer, DET: Double embryo transfer



**Figure 4. Transfer characteristics and results in Fresh, Frozen and PGT cycles**

ET: Embryo transfer, SET: Single embryo transfer, LBR: Live birth rate, PGT: Preimplantation genetic test



### Data from international patients

Nine centers completed the question block about couples who did not reside in Turkey but were undergoing ART treatment here. A total of 1552 cycles were performed [83.6% only IVF or ICSI, 16.4% pre-implantation genetic diagnosis (PGD)]. The top five countries where these couples reside were Russia (29.6%), Germany (7.4%), Iraq (4.6%), Uzbekistan (3.1%), and Syria (1%). The remaining 851 couples (56.2%) were from other countries. The reason for choosing a foreign country for treatment was enquired about. According to the survey, only 68 (4.4%) couples chose Turkey because of the treatment cost benefit.

### Discussion

This was a descriptive survey study including data from 25 infertility centers operating in Turkey with data collected for the year 2019. Our purpose was not to compare centers or treatment modalities but to provide an overview of demographic properties and ART treatment in Turkey, using anonymous data. According to the Turkish Statistical Institute, women of reproductive age (between 15-45 years old) make up 26.5% of the population in Turkey, and 1,194,423 births took place in 2019 (7). In the same year, a total of 18,127 ETs were carried out in 25 centers, and 43.0% of these transfers included fresh, 45.2% frozen cycles, and 1.8% PGT cycles. In total, 64.6% ETs were single ETs and the singleton LBR among all deliveries was 87.5%. As for the IUI cycles in the same year, 1407 cycles were initiated and there were 195 clinical pregnancies and 150 deliveries occurred.

As demonstrated in international reports, ART applications has increased compared to prior years (1,2). To exemplify from (HFEA) data, the number of cycles, around 30,000 in the 90s and 40,000 in the early 2000s, is approaching approximately 70,000 in 2019 (1). Although the ultimate success of ART/MAR treatments is expressed as the take-home baby rate, the treatment processes must be within the scope of excellence and ethical health care, without increasing maternal and antenatal morbidity. In this context, annual international statements are imperative to regulate treatment planning.

In 2021 and 2022, annual reports for 2019 on infertility treatments applied in the United Kingdom and the United States were published by HFEA and SART, respectively (1-3). According to SART reports, when all cycles other than donation cycles are considered, LBRs per egg collection attempt in patients under 35 years old, 35-37 years old, 38-40 years old, 41-42 years old and over 42 years old, were 55%, 41%, 26.8%, 13.4%, and 4.3%, respectively. Of these deliveries, preterm delivery rates varied between 12.3% to 15.7% which is lowest in women under 35 years old and highest in women over 42 years old. Finally, the number of transferred embryos varies between 1.2 (under 35

years old) and 2.1 (over 42 years old) (2). In the present study we could not analyze transferred embryo or gestational week at delivery according to different age groups. However, the LBR per aspiration in fresh cycles was 28.5% in women under 35 years of age, 20.3% in the 35-39 age group, and 7.5% for >40 years group. The LBR per thawings in frozen cycles was 45.4% in women under 35 years of age, 40.7% in the 35-39 age group, and 22.3% for >40 years group. According to the HFEA report relating to the same year, LBRs per ET in different age groups ranged from below 5% (43 years and above) to 32% (under 35 years old). Other important points in the HFEA report were that single ET constituted 75% of all transfer cycles, multiple births were reduced to 6% of all births (28% in the 1990s), and patients over 40 years of age have a rate of 21% in all cycles (almost doubled compared to 1990s) (1). In the present study, we found that the single ET rate was 65.3% of all cycles, and the multiple birth rate was 13.9% among all deliveries.

In these annual reports, it is crucial to demonstrate to what extent or rate ART treatments are covered by private insurance or the national social healthcare system. For example, US national-registry ART practices data revealed significant discrepancies in outcomes based on state-obliged policies and insurance treatment coverage rates. Compared with states without compulsory insurance coverage for ART, states with comprehensive jurisdiction have lower rates of multiple pregnancies (especially three or more) and fewer ET per cycle (8,9). As an explanation for these statements, it was presumed that in states where treatment costs are not required to be covered, it is a challenge to accomplish a "successful" result from the first time and, therefore, to transfer more embryos per cycle (8). A similar situation can be investigated in Turkey by adding a couple of parameters to the cycle outcomes data collected in upcoming years.

The biggest strength of our study was that, to the best of our knowledge, this study is the first to include a large number of ART centers in Turkey that allows a panoramic view of the status of ART practice through aggregated anonymous data. Next, the survey was prepared in accordance with ESHRE EIM consortium. Moreover, it is a promising start to monitor the trends in ART treatment in Turkey over the upcoming years, if the survey is carried out annually.

### Study limitations

The most significant limitation of our study is the low participation rate of around 15%. Other limitations are the scarcity of data for fertility preservation which has gained popularity and the lack of detailed allocation of treatment attributes according to specific age groups, such as the number of transferred embryos, multiple pregnancy rate, and

distribution by the week of birth. We hope to overcome these limitations in future surveys.

## Conclusion

This nationwide survey describes the demographic distributions and clinical results of ART practices in Turkey in 2019. Our results are in parallel with those reported by international institutions and organizations. This study is the first step towards developing an annual overview of ART practices in Turkey. We hope it will attract more participants, include more detailed data in the upcoming years and will serve to inform patients, health care professionals working in the field of ART and policymakers and improve ART practice in our country.

**Ethics Committee Approval:** *The study was approved by the Koç University Ethics Committee (approval number: 2022.386. IRB1.141, date: 07.11.2022).*

**Informed Consent:** *The authors confirm that fully informed, freely given and written consent to participate were obtained from all participants (cohort) in the present study.*

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**Conflict of Interest:** *No conflict of interest is declared by the authors.*

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