

<https://doi.org/10.37800/RM.1.2024.8-16>

УДК: 618.5-089.888.14-7

Assisted Reproductive Technologies in Kazakhstan (2020 National ART Registry data)

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ABSTRACT

Relevance: The article presents aggregate data on the programs of assisted reproductive technologies (ART) implemented in 2020 in Kazakhstani clinics specializing in treating infertility using ART.

The study aimed to analyze the structure and results of ART cycles conducted and Registered in the Republic of Kazakhstan from 1 January 2020 to 31 December 2020.

Materials and Methods: A retrospective analysis of data from reports of 17 ART clinics in Kazakhstan, which were voluntarily submitted to the Kazakhstan Association of Reproductive Medicine (KARM), was conducted. The reports included information on IVF cycles, ICSI, embryo cryopreservation, oocyte donation (OD), surrogacy, and preimplantation genetic testing (PGT).

Results: The total number of ART cycles available for analysis in 2020 was 17,743, resulting in the birth of 5,932 newborns. The accessibility of ART treatment amounted to 952 cycles per 1 million population.

Analysis of the ART structure revealed that IVF cycles accounted for 11.9% of all ART cycles in clinics in Kazakhstan, while ICSI was 33.4%. A combined method of fertilization, using both IVF and ICSI (50/50), was performed in 13.0% of cycles. Frozen embryo transfer (FET) was conducted in 47.4% of cycles, while OD programs were carried out in 11.4% of cycles and PGT in 5.3% of cycles.

The pregnancy rate per aspiration in 2020 was 20.9% for IVF cycles, 20.4% for ICSI cycles, and 42.5% for FET cycles. When calculated per transfer, the pregnancy rate was 38.5% for IVF cycles and 39.5% for ICSI cycles. For OD programs, the pregnancy rate per aspiration was 50.6%. In 2020, live birth rates were 30.7% in fresh IVF cycles, 32.4% in ICSI cycles, 33.4% in FET cycles, and 42.0% in OD programs.

In 2020, 1,103 programs were conducted in Kazakhstan. The Registry of pregnant women and women of fertile age reported the pregnancy rate of 46%, the live birth rate of 26%, and the frequency of multiple births of 21.8%.

Conclusion: According to the Registry, the number of ART programs increased by 1.1% in 2020 vs. the previous year. The negative impact of COVID-19 on this indicator is unquestionable. The pregnancy and live birth rates remained stable and corresponded to the average ESHRE indicators.

Keywords: assisted reproductive technologies (ART), 2020 ART report, IVF, ART accessibility

How to cite: Lokshin VN, Suleimenova MD, Karibaeva ShK, Dzhusubaliyev NM, Yakhyarova MP, Mukhamedyarov DA, Akhmetova AA, Kovaleva NK, Nigmatova NP, Chalova LR, Aripova RS, Imtosimi DG, Lapina EV, Otarbaev MK, Basarova GJ, Begaidarova AB. Assisted Reproductive Technologies in Kazakhstan (National Registry Data, 2020). *Reprod Med.* 2024;(1):8-16.

<https://doi.org/10.37800/RM.1.2024.8-16>

Вспомогательные репродуктивные технологии в Казахстане (данные Национального регистра ВРТ за 2020 г.)

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АННОТАЦИЯ

Актуальность: В статье представлены совокупные данные о реализованных программах вспомогательных репродуктивных технологий (ВРТ) в 2020 году в клиниках Казахстана, специализирующихся на лечении бесплодия при помощи ВРТ.

Цель исследования – анализ структуры и результатов циклов ВРТ, проведенных и зарегистрированных в Республике Казахстан с 1 января по 31 декабря 2020 года.

Материалы и методы: Произведен ретроспективный анализ данных отчетов 17 клиник ВРТ Казахстана, представленных на добровольной основе в Казахстанскую Ассоциацию Репродуктивной Медицины (КАРМ). Отчеты включали информацию о циклах ЭКО, ИКСИ, крио-переносах эмбрионов, донорстве ооцитов (ДО), суррогатном материнстве и преимплантационном генетическом тестировании (ПГТ).

Результаты: Общее число доступных анализу циклов ВРТ за 2020 г., включенных в отчет составило 17 743, в результате которых родились 5 932 новорожденных. Доступность лечения с помощью ВРТ составила 952 циклов на 1 млн населения.

Анализ структуры ВРТ выявил, что доля ЭКО в клиниках РК составила 11,9% от всех циклов ВРТ, доля ИКСИ — 33,4%, смешанный способ оплодотворения ЭКО/ИКСИ – 50/50 в выполнен в 13,0% циклов; перенос размороженных эмбрионов (FET) проведен в 47,4%, программа ДО была выполнена в 11,4% циклов, ПГТ – в 5,3% циклов.

Частота наступления беременности в расчете на пункцию составила по итогам 2020 года в циклах ЭКО – 20,9% на трансвагинальную пункцию, в расчете на перенос – 38,5%, в программе ИКСИ – 20,4% на пункцию, в расчете на перенос – 39,5%, в программе FET – 42,5%, в программе ДО – 50,6%. Показатель частота живорождения в 2020 году в свежем цикле ЭКО составила – 30,7%, в программах ИКСИ – 32,4%, FET – 33,4%, ДО – 42,0%.

В Республике в 2020 году было проведено – 1103 программ. Частота наступления беременности по данным РБ и ЖФВ составила – 46%, а частота живорождения – 26%. Частота многоплодия – 21,8%.

Заключение: В соответствии с данными регистра, в 2020 году количество программ ВРТ увеличилось на 1,1% по сравнению с предыдущим годом. Негативное влияние COVID-19 на исследуемый показатель не вызывает сомнений. Частота наступления беременности и живорождения стабильна и соответствует средним показателям ESHRE.

Ключевые слова: вспомогательные репродуктивные технологии (ВРТ), отчет по ВРТ за 2020 г., ЭКО, доступность ВРТ.

Для цитирования: Локшин В.Н., Сулейменова М.Д., Карибаева Ш.К., Джусубалиев Н.М., Яхьярова М.П., Мухамедьяров Д.А., Ахметова А.А., Ковалева Н.К., Нигматова Н.П., Чалова Л.Р., Арипова Р.С., Имтосими Д.Г., Лапина Е.В., Отарбаев М.К., Басарова Г.Ж., Бегайдарова А.Б. Вспомогательные репродуктивные технологии в Казахстане (данные Национального регистра, 2020 г.) // Репрод. Мед. – 2024. – №1(58). – С. 8-16. <https://doi.org/10.37800/RM.1.2024.8-16>

Қазақстандағы қосалқы репродуктивті технологиялар (Ұлттық ART тізілімінің 2020 деректері)

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АНДАТПА

Өзектілігі: Мақалада 2020 жылы қосалқы репродуктивті технологиялар (ҚРТ) көмегімен бедеулікті емдеуге маманданған Қазақстан клиникаларында ҚРТ іске асырылған бағдарламалары туралы жиынтық деректер келтірілген.

Зерттеудің мақсаты – 2020 жылғы 1 қаңтардан бастап 2020 жылғы 31 желтоқсанға дейін Қазақстан Республикасында жүргізілген және тіркелген ҚРТ циклдерінің құрылымы мен нәтижелерін талдау.

Материалдар мен әдістері: Қазақстандық Репродуктивті медицина қауымдастығына (ҚАРМ) ерікті негізде ұсынылған Қазақстан ҚРТ 17 клиникасының есептеріне ретроспективті талдау жүргізілді. Есептерде ЭҚҰ, ICSI, эмбрионды крио тасымалдау, ооцит донорлығы (ОД), суррогат ана және имплантацияға дейінгі генетикалық тестілеу (PGT) циклдары туралы ақпарат болды.

Нәтижелері: Есепке енгізілген 2020 жылғы талдауға қол жетімді ҚРТ циклдерінің жалпы саны 17 743 құрады, нәтижесінде 5 932 жаңа туған нәресте дүниеге келді. ҚРТ көмегімен емдеудің қол жетімділігі 1 миллион тұрғынға 952 циклды құрады.

ҚРТ құрылымын талдау ҚР клиникаларындағы ЭҚҰ үлесі барлық ҚРТ циклдерінің 11,9%, ИКСИ үлесі – 33,4%, ЭКО/ИКСИ-50/50 ұрықтандырудың аралас тәсілі циклдердің 13,0% орындағанын; еріген эмбриондарды (FET) тасымалдау 47,4% - да жүргізілгенін, ДО бағдарламасы циклдердің 11,4% орындағанын, PGT-циклдердің 5,3%.

Пункция есебінде жүктіліктің болу жиілігі 2020 жылдың қорытындысы бойынша ЭҚҰ циклдарында – трансвагинальды пункцияға – 20,9%, тасымалдау есебінде – 38,5%, ИКСИ бағдарламасында пункцияға – 20,4%, тасымалдау есебінде – 39,5%, FET бағдарламасында – 42,5%, бағдарламада – 50,6% құрады. Көрсеткіш тірі туылу жиілігі 2020 жылы ЭҚҰ жаңа циклінде – 30,7%, ИКСИ бағдарламаларында – 32,4%, FET – 33,4%, 42,0% дейін құрады.

Республикада 2020 жылы 1103 квоталық бағдарламалары жасалынды. РБ және ЖФВ деректері бойынша жүктіліктің болу жиілігі – 46%, ал тірі туылу жиілігі – 26% құрады. Көпұрықтылық жиілігі – 21,8%.

Қорытынды: тіркелім деректеріне сәйкес 2020 жылы ҚРТ бағдарламаларының саны өткен жылмен салыстырғанда 1,1% - ға өсті. COVID-19-ның зерттеу көрсеткішіне теріс әсері күмән тудырмайды. Жүктілік және тірі туылу жиілігі тұрақты және ESHRE орташа көрсеткіштеріне сәйкес келеді.

Түйінді сөздер: қосалқы репродуктивтік технологиялар (ҚРТ), 2020 жылға арналған ART есебі, ЭҚҰ, қолжетімділік.

Introduction: According to the latest World Health Organization (WHO) report, approximately one-sixth of couples will experience infertility problems during their lifetime, which is approximately 17.5% of the adult population [1]. Data from the Multiple Indicator Cluster Survey (MICS) indicate that infertility was defined by self-reported sexually active women aged 15 to 44 years who reported having tried to become pregnant for two years or more without success. The percentage of infertility varies depending on the age group: for the age group 15-19 years – 0%; 20-24 years – 0.9%; 25-29 years – 2.0%; 30-34 years – 2.6%; 35-39 years – 4.4%; 40-44 years – 4.9% [2].

Since 2008, KARM, under a particular IT program proposed by ESHRE, has been collecting data on ART cycles performed in the Association's member clinics and sending them to the European IVF Monitoring Consortium (<https://www.eshre.eu/eim>). This report (2020) is the fourth year it has been published in Reproductive Medicine.

Thirty-one ART clinics operating in the RK today offer almost all modern assisted reproductive technologies and methods for diagnosing and treating infertility existing in the world.

Since 2010, programs within the guaranteed volume of medical care have been implemented in Kazakhstan. Starting from 2021, K.-J. Tokayev, the President of the Republic of Kazakhstan, initiated the state program «Ansagan Sabi», which increased the number of allocated quotas by almost 7 times, to 7,000 per year. KARM constantly monitors the implementation of this program. Over 27 years, more than 29,000 children were born in the country after the successful implementation of ART programs, including more than 7,000 in quota programs (data as of November 1, 2022).

The frequency of infertile marriage in the Republic of Kazakhstan ranges from 12.0 to 15.5% [3]. Childlessness caused by infertility has a significant impact on both demographic indicators, the psycho-emotional and physical health of the nation, and the socio-economic development of the country [4]. As the incidence of infertility increases, the

need for the use of assisted reproductive technologies also increases [5].

The study aimed to analyze the structure and results of ART cycles conducted and Registryed in the Republic of Kazakhstan from January 1, 2020, to December 31, 2020.

Materials and Methods: A retrospective analysis of data from reports from ART clinics voluntarily submitted to the Kazakhstan Association of Reproductive Medicine (KARM) was conducted. Reports included data on IVF cycles, ICSI, embryo cryopreservation, surrogacy, preimplantation genetic testing (PGT), and oocyte donation (OD). Due to the absence of a mandatory state ART registry, some data from IVF clinics still needed to be provided. The figures (in absolute numbers and percentages) represent aggregated data for the year.

Data collection for the current registry was conducted using the form recommended by the European Society of Human Reproduction and Embryology (ESHRE) [6].

The accessibility of ART for citizens of the country was calculated by dividing the number of cycles by the country's population. The pregnancy and live birth rates were calculated by dividing the total number of pregnancies or deliveries by the number of transvaginal punctures or embryo transfers.

Registry participants, number of ART cycles

The 2020 report included 17 ART clinics (60.7%) from 28 ART centers operating in Kazakhstan.

The total number of ART cycles available for analysis performed in ART centers of the Republic of Kazakhstan in 2020 was 17,743 (in 2019 – 15,888 cycles; +1.1% compared to 2019). As of January 1, 2020, according to the Statistics Committee of the Republic of Kazakhstan (<http://taldau.stat.gov.kz>), the population of the Republic of Kazakhstan amounted to 18 million 632.2 thousand people. Since 2010, data on 72,145 ART cycles have been collected. 952 ART cycles were performed per 1 million people (Figure 1).

In 2020, out of 17 clinics participating in the report, 5 were in Nur-Sultan, 5 in Almaty, 3 in Shymkent, and 1 in Aktobe, Taraz, Atyrau, and Karaganda.

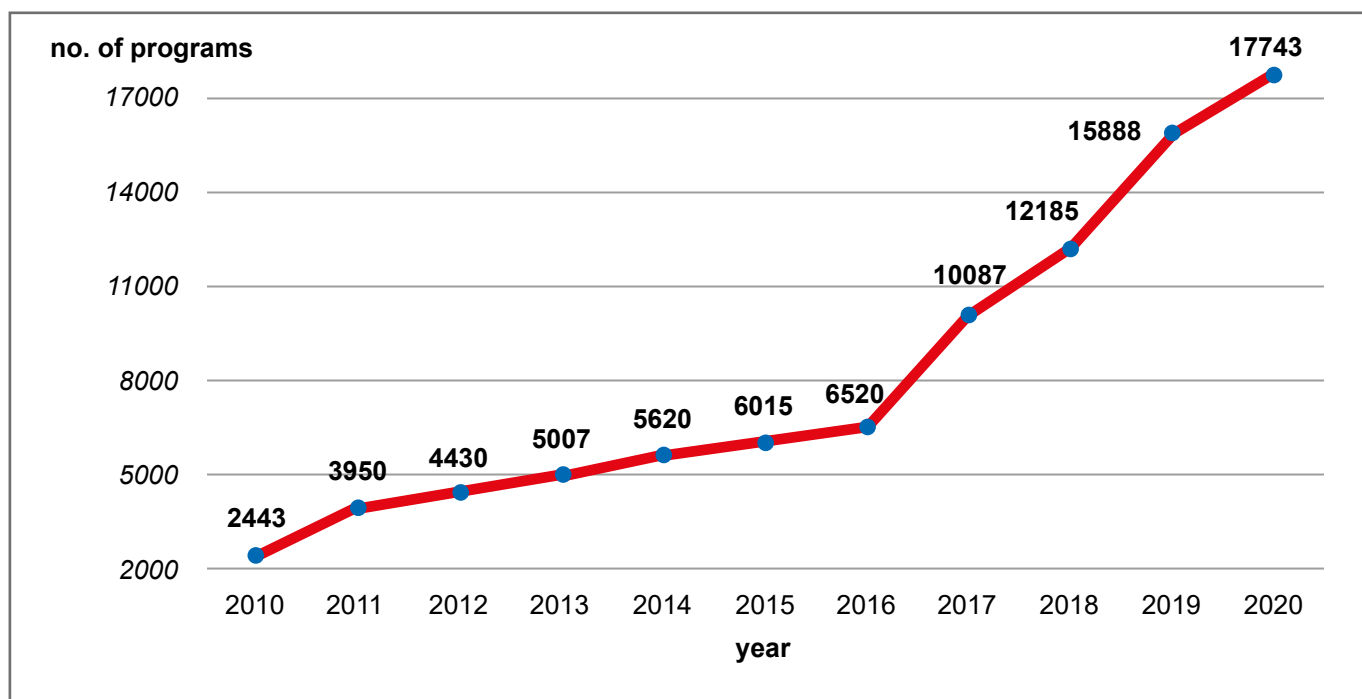


Figure 1 – Dynamics in the number of ART cycles per year in the Republic of Kazakhstan, 2010-2020

Results:

Structure of ART cycles. Analysis of the distribution of programs based on utilized methods in 2020 revealed that the proportion of IVF in clinics in Kazakhstan was 11.9% (in 2019 – 17.7%) of all ART cycles, the proportion of ICSI was 33.4% (in 2019 – 36.0%); (in the ESHRE report IVF 16.2%, ICSI 39.7%), the combined method of fertilization IVF/ICSI – 50/50 in Kazakhstan was applied in 13.0% of cycles; frozen embryo transfer (FET) program was conducted in 47.4% of cycles (in 2019 – 31.3%; according to ESHRE data – 30.7%), oocyte donation (OD) – in 11.4% of cycles (in 2019 – 10.7%; according to ESHRE data – 8%), preimplantation genetic testing

(PGT) – in 5.3% of cycles (in 2019 – 4.1%; according to ESHRE data – 4.8%).

The volume of implemented programs involving the use of donor sperm amounted to 382 (2.1%) in 2020, representing an increase compared to 2019, when such programs numbered 327 (3.9%). From this total, 91 cases (0.6%) included the use of surgically obtained sperm, significantly fewer than the 217 cases (2.6%) in 2019.

Within the oocyte donation (OD) program, 1586 embryos were transferred in 2020 vs. 1771 embryo transfers in 2019. As a result, 802 pregnancies occurred, representing 50.6% of the total transferred embryos (50.9% in 2019). Of these pregnancies, 681 were completed with deliveries, accounting for 42.9% of the total (38.1% in 2019) (Table 1).

Table 1 – Comparative data on the dynamics in the number of ART programs in the Republic of Kazakhstan (2010-2020)

Year	The number of cycles							Annual growth (%)	Cycles/ million population
	IVF	ICSI	FET	DO	PGT	S	Total		
2010	1282	348	289	298	58	167	2443		149,8
2011	1785	952	564	302	85	262	3950	38,2%	236,9
2012	1780	1086	826	358	57	323	4430	10,8%	261,9
2013	1403	1699	980	591	82	252	5007	11,5%	291,7
2014	1354	2055	1269	484	179	279	5620	10,9%	322,7
2015	1283	2516	1210	600	132	274	6015	6,6%	340,4
2016	1120	2835	1449	633	195	288	6520	7,7%	364,0
2017	1632	4186	2542	995	475	257	10087	35,4%	583,0
2018	1555	4955	3489	1187	652	347	12185	17,2%	628,0
2019	2750	5598	4860	1771	543	366	15888	23,3%	835,1
2020	2072	5157	7305	1996	920	293	17743	+1,1%	952

Number of transferred embryos. In 2020, within IVF/ICSI cycles, the proportion of cases involving selective embryo transfer (SET) was 63.1% (compared to 48.8% in 2019), indicating a 14.2% increase from 2019.

Transfer of 2 embryos occurred in 36.7% of cases (compared to 43.7% in 2019), representing a decrease of 7.0% from 2019, while transfer of 3 embryos occurred in 0.2% of cases (compared to 7.4% in 2019). There were no instances of transferring 4 or more embryos, as in 2019.

According to data provided by the European Society of Human Reproduction and Embryology (ESHRE) in 2019 for fresh cycles, single embryo transfer was performed in 50.7% of cases, two embryos in 45.1%, three embryos in 3.9%, and four embryos in 0.3% of cases.

Pregnancy. In 2020, we obtained data on 7367 pregnancies. In the IVF program, PR in 2020 was as follows: per aspiration – 20.9% (according to ESHRE data 25.5%), per transfer – 38.5% (according to ESHRE – 34.1%) (in 2019 – 22.2% and 34.5%). In the ICSI program, these indicators were 20.4% and 39.5%, respectively (in 2019 – 21.1% and 38.1%) (according to ESHRE, 22.5% and 32.1%).

In the frozen embryo transfer program, the PR per embryo transfer was 42.5% (in 2019 – 43.9%) (according to ESHRE, 33.4%). In programs involving PGT, the PR per embryo transfer was 53.2% (in 2019 – 52.2%).

Numbers of embryos transferred. The PR following embryo transfer at the cleavage stage (day 3) compared to transfer at the blastocyst stage (days 5-6) is lower and amounted to: in fresh IVF and ICSI cycles – 28.5% and 43.6% (in 2019 – 26.3% and 41.6%), in cycles with FET – 39.7% and 46.3% (in 2019 – 34.6% and 46.7%), in cycles with donor oocytes – 31.0% and 53.0% (in 2019 – 37.9% and 52.5%).

The PR in IVF/ICSI cycles after the transfer of 1 embryo was 37.3% (in 2019 – 41.6%), after the transfer of 2 embryos was 42.0% (in 2019 – 44.8%), and after the transfer of 3 embryos, was 55.6% (out of 9 transfers, resulting in 5 pregnancies) (in 2019 – 14.1%). In FET cycles, the PR after the transfer of 1 embryo was 42.6% (in 2019 – 44.0%); after the transfer of 2 embryos was 42.4% (in 2019 – 47.6%); and after the transfer of 3 embryos, it was 25.0% (2 pregnancies after 8 transfers). In donor programs, the PR after the transfer of 1 embryo was 50.2% (in 2019 – 48.0%), after the transfer of 2 embryos was 63.0% (in 2019 – 47.6%), and after the transfer of 1 embryo, was 47.8% (in 2019 – 44.0%), after the transfer of 2 embryos was 63.0% (in 2019 – 55.3%).

Age of Patients and IVF Outcomes. In the patient group aged 35-39 years, the pregnancy occurrence rate (PR) and live birth rate (LBR) in IVF programs were 22.6% and 18.6% (in 2019 – 24.2% and 18.1%), and in ICSI programs 21.0% and 18.3% (in 2019 – 23.3% and 21.6%), respectively, which were lower compared to these indicators in women under 34 years old in IVF 28.9% and 22.8% (in 2019 – 26.0% and 19.6%) and slightly higher in ICSI cycles 27.0% and 20.8% (in 2019 – 22.1% and 17.5%). In women over 40 years old, the PR and LBR were half as low: in IVF cycles – 8.4% and 6.2% (in 2019 – 9.3% and 4.7%), respectively; in ICSI cycles – 8.0% and 6.2% (in 2019 – 13.7% and 8.2%), respectively.

PR and LBR were higher in all age groups during frozen embryo transfer than in IVF and ICSI cycles. In particular, in women under 34 years old, the PR and LBR were 48.4% and 39.6% (in 2019 – 52.1% and 36.7%), in women aged 35-39 years – 38.6% and 30.2% (in 2019 – 44.7% and 27.7%), and in women over 40 years old – 32.4% and 21.7% (in 2019 – 27.4% and 18.0%), respectively.

For comparison, according to ESHRE data, in IVF cycles, the PR for women under 34 years old was 30.8%, between 35-39 years old – 25.4%, and for women over 40 – 13.6% (LBR – 25.1%, 19.0%, 7.8%); in ICSI cycles, the PR was 27.9%, 22.3%, and 11.2% (LBR – 22.1%, 16.1%, 6.3%), respectively.

High PR was observed in all age groups in the OD program (PR was 51.4%, 50.9%, and 50.1%, respectively). However, even in this program, the negative effect of a woman's age on the primary outcome was confirmed: thus, completion of pregnancy with deliveries occurred in 44.8%, 41.6%, and 42.9% of cases, respectively (ESHRE, PR – 43.6%, 44.9%, 43.2%, and LBR – 33.4%, 33.2%, 29.5%, respectively) (Figures 2 and 3).

Surrogacy. The total number of programs utilizing surrogacy in 2020 was 293, which accounts for 1.2% of the total number of ART procedures. As a result, 135 pregnancies occurred (46.2%), and 108 pregnancies (36.9% of the total number of transfers) ended with childbirth defined as 22 weeks and beyond.

Childbirth and other pregnancy outcomes. In the reports, all pregnancy terminations starting from 22 completed weeks are classified as «births.»

There were 5932 births at 22 weeks gestation or later (in 2019 – 4042), corresponding to 1.3% of all newborns born in the Republic of Kazakhstan (the total number of newborns in 2020 was 426,824) [7].

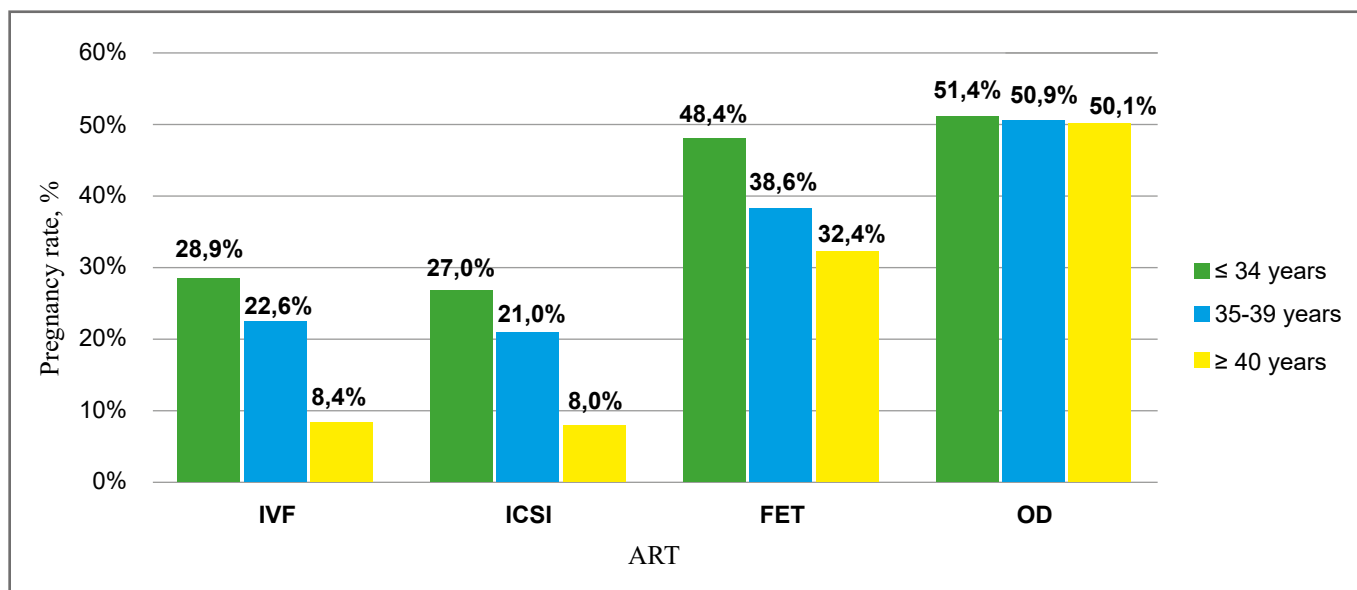


Figure 2 – Pregnancy rates in different age groups (RK, 2020)

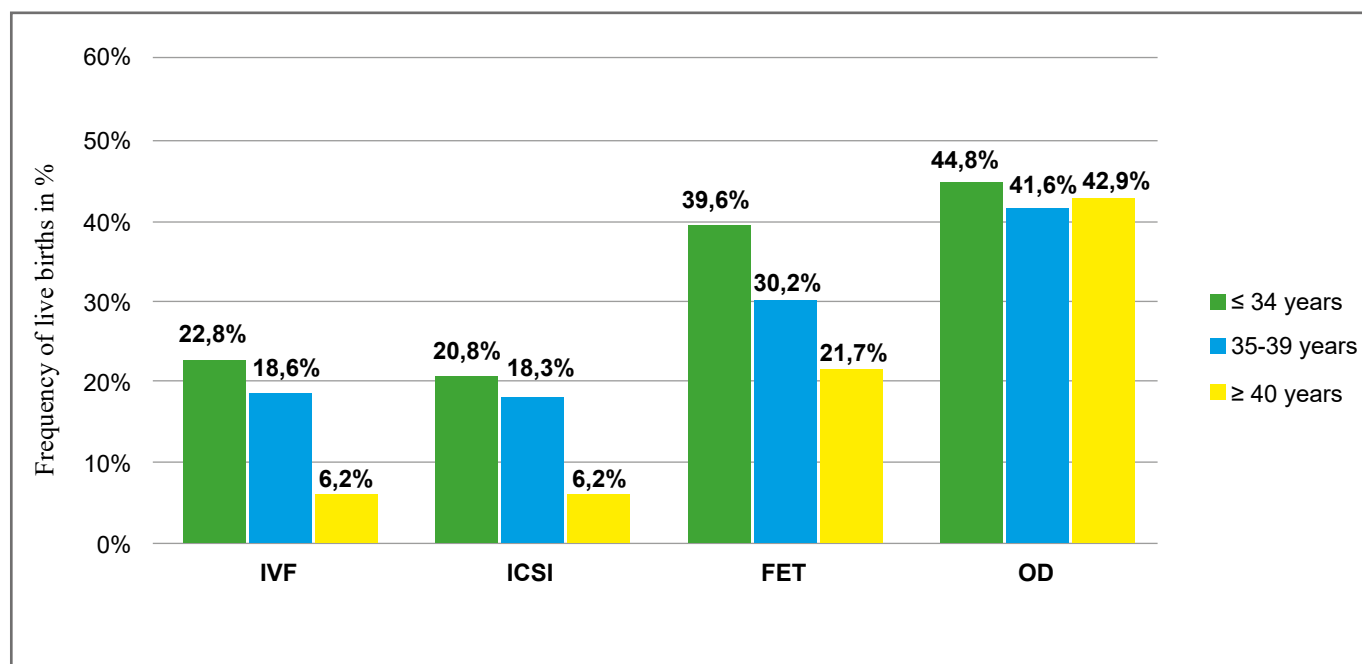


Figure 3 – Frequency of live births after ART depending on the woman's age (RK, 2020).

IVF - in vitro fertilization; ICSI - intracytoplasmic sperm injection; FET - frozen embryo transfer; OD - oocyte donation.

Multiple births. The frequency of multiple births in IVF and ICSI programs was 8.3% (varies in clinics in Kazakhstan from 4 to 15%) of all known births; after transfer of thawed embryos – 9.8% (varies in clinics in Kazakhstan from 4 to 16%); in the OD programs – 6.5%, in the surrogacy programs – 13.4%. (according to ESHRE twins – 12.4% in fresh IVF and ICSI cycles, 9.4% in cryopreservation).

Preimplantation genetic testing (PGT). In 2020, PGT in ART centers was carried out in 920 cycles (in 2019 – in 869 cycles), pregnancy occurred in 489 cases – 53.1% (in 2019 – 63.0%), and 388 pregnancies ended with childbirth at 22 weeks. And more – 42.1% (in 2019 – 43.8%).

Discussion: This study analyzed the structure and outcomes of Registryed ART cycles performed in Kazakhstan. The findings were compared with the 22nd annual report of the European IVF Monitoring Consortium under the auspices of ESHRE, which compiled data on ART and IUI reported by 39 participating European countries in 2019.

When comparing the effectiveness of IVF treatment with the results of EIM-ESHRE, the effectiveness of pregnancy rates per aspiration and transfer after IVF were slightly lower in RK – 20.9% and 38.5%, respectively, according to ESHRE – 28.7% and 41.6 %, respectively. Results after ICSI in European countries reached 20.4% and 37.4% over the selected period, while in the RK, they were 21.7% and 39.5%, respectively. After cryotransfer with their oocytes, the pregnancy rate results according to EIM were 33.0%, and in the RK, 42.5%, which is 10% higher than in the ESHRE report. In the program with additional education, the results of the Republic of Kazakhstan are similar to European data – 50.6% per transfer.

In 2020, 1,103 programs were conducted in our country. According to the «Registry of pregnant women and women of fertile age», the pregnancy rate was 46%, the live birth rate was 26%, and the frequency of multiple births was 21.8%.

According to ESHRE, the frequency of multiple pregnancies (twins) was 12.4%, 1.1% less than the exact figure in the RK. In the ESHRE registry, IVF and ICSI programs show a strong trend towards fewer embryos being transferred: 1, 2, and 3 embryos are transferred in 64.3%, 35.5%, and 0.2% of

all procedures, respectively. A similar trend was noted in our country: 61.3%, 38.4%, 0.2% and 0%.

Conclusion: According to the registry data, in 2020, the number of ART programs increased by 1.1% compared to the previous year. The characteristics associated with the participation of specific medical centers in this report do not allow for an exact determination of whether the established decrease in the total number of ART cycles results from restrictions imposed due to the COVID-19 epidemic in 2020. These restrictions affected the provision of planned medical care, including ART programs. However, the negative impact of this factor on the investigated indicator is unquestionable.

The proportion of transfers of more than three embryos within ART programs decreases annually; in 2020, it amounted to 0.02%. It should be noted that during this period, the Order of October 30, 2009, No. 627 «On the Approval of the Rules for the Implementation of Assisted Reproductive Methods and Technologies» of the Ministry of Health allowed the transfer of three embryos, provided that the patient gave appropriate consent. The Order of December 20, 2020, No. 21816, «On the Approval of the Rules and Conditions for the Implementation of Assisted Reproductive Methods and Technologies» of the Ministry of Health, allows the transfer of no more than two embryos.

The pregnancy rate in 2020, in IVF cycles, was 20.9% per aspiration and 38.5% per transfer; in ICSI programs, it was 20.4% per aspiration and 39.5% per transfer; in FET, it was 42.5%; in OD programs, it was 50.6%. In 2020, the live birth rates were 30.7% after fresh IVF cycles, 32.4% in ICSI programs, 33.4% in FET, and 42.0% in OD. The pregnancy and live births rates were stable and corresponded to the average indicators of ESHRE.

The Registry data can be used to objectively assess the results of reproductive medicine in the country and forecast its development. The next step in developing the country's ART registry should be its mandatory prospective maintenance.

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Funding: Authors declare no funding of the study.

Conflict of interest: Authors declare no conflict of interest.

Transparency of the study: Authors take full responsibility for the content of this manuscript.

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