



Mini Review

Volume 22 Issue 3 - July 2022  
DOI: 10.19080/JGWH.2022.22.556089

J Gynecol Women's Health

Copyright © All rights are reserved by OG Boychuk

# Infertility - Diagnosis, Treatment in Senior Reproductive Age Women



OG Boychuk\* and US Dorofeeva

Ivano-Frankivsk National Medical University, Department of Obstetrics and Gynecology of Postgraduate Education, Ivano-Frankivsk, Ukraine

Submission: June 29, 2022; Published: July 05, 2022

\*Corresponding author: OG Boychuk, Ivano-Frankivsk National Medical University, Department of Obstetrics and Gynecology of Postgraduate Education, Ivano-Frankivsk, Ukraine

## Resume

**Aim:** The aim of the study was to determine the features of infertility and its treatment by ART in women of older reproductive age.

**Materials.** The analysis of 658 histories of patients of IVF programs for 2015-2019 was carried out. The patients were divided into 2 groups: the main - 333 women aged 35 and over, the control - 325 women under 35 years.

**Results:** There is a tendency to increase the share of women of older age category: in 2019 the share of women aged 35 and over increased by 6.1% compared to 2015 (from 47.6% to 53.7%). Older women were much more likely to be forced to use oocyte donation (14.2% vs. 3.7% before age 35). After 40 years, this method of ART was used by 23.4% of patients. In 48.0% of older women, the cause of infertility is marked "only another female factor" (endocrinological disorders, ovarian insufficiency, etc.). After 35 and 40 years, the share of women with primary infertility decreases (34.1% and 27.4% against 48.0% before the age of 35) and the share of those who suffer from infertility for more than 5 years increases. Decreased ovarian reserve was diagnosed in 48.0% of patients after 35 years, after 40 years - 57.3%, which corresponds to the indicators of FSH increase and AMG decrease. A quarter (24.0%) of women after the age of 35 already had one unsuccessful attempt at IVF, and 12.6% - 2 or more attempts (after 40 years - 16.9%). After 35 years, the rate of clinical pregnancies per started cycle (30.0% vs. 39.1%) and live births (21.1% vs. 30.2%) significantly decreases. After 40 years, these 2 indicators are 21.8% and 13.7%.

**Conclusion:** Given the increasing proportion of women who resort to ART in older reproductive age, as well as a number of factors that worsen the prognosis of ART, among which the reduction of ovarian reserve is the least controlled, it is important to find methods to optimize training of such patients to obtain quality mature oocytes.

**Keywords:** Infertility; Assisted reproductive technologies; Senior reproductive age; Ovarian reserve; *In vitro* fertilization

## Introduction

Infertility is a common phenomenon, according to recent publications, its prevalence in the general population ranges from 9 to 18% [1,2]. It is reported that 33-41% of infertility cases are related exclusively to the female factor, the male factor accounts for 25-39% of the problem, and 9-39% - due to a combination of both male and female factors [3].

A common etiology of female infertility is ovulation disorders such as polycystic ovary syndrome, hypothalamic dysfunction, premature ovarian failure, tubal infertility, endometriosis and / or causes of cervix and cervix, while male infertility is mainly associated with impaired sperm function, sperm blocking, hormonal imbalance, malignant neoplasms, infections, antisperm antibodies [4]. In addition, according to various estimates, approximately 30% of infertile couples worldwide are diagnosed

with unexplained or idiopathic infertility, and this clinical problem is defined as the absence of an obvious cause of infertility in couples [5]. Among the causes of infertility in the started cycles in Ukraine in 2019, combined factors were more often registered (27.60%), another female factor (23.84%), then - only the tubal factor (14.61%) and only the male factor (14, 15%), idiopathic infertility (6.71%) [6].

Infertility is expected to increase in the future, so a comprehensive diagnostic assessment of infertility is crucial to improve targeted prevention and treatment outcomes [7]. Assisted reproductive technologies (ART), mainly intrauterine insemination (IUI) and *in vitro* fertilization (IVF), have helped many couples overcome infertility. Millions of children are born with ART worldwide, and now account for > 4% of births in some

European countries [2]. In Ukraine, as a result of ART for the period 1999-2019, 82,895 children were born [6].

Rationale for the study. The mother's older reproductive age is an important social and clinical problem. Currently, the proportion of women who postpone childbirth until the end of the 3rd - beginning of the 4th decade of life has increased significantly, especially in Western societies [8]. Such trends are observed in all parts of the world, including Canada and Europe, with one of the highest average ages of women giving birth for the first time in Italy - 30.6 years [9,10]. Decreased fertility in old age (after 35 years) can be explained, on the one hand, by the gradual depletion of ovarian reserve, and on the other - by the progressive decline in egg / embryo competence, defined as the ability to give birth to living children [11].

There is a persistent misconception that assisted reproductive technologies can turn back the "biological clock" [12], but the success rate of IVF decreases significantly when women enter the 5th decade of life [13]. The aim of the study was to determine the features of infertility and its treatment by ART in women of older reproductive age.

### Materials and Methods

An analysis of 658 patient histories of IVF programs for 2015-2019. Given the purpose and objectives of our study for further analysis, we divided patients into 2 groups: the main group - 333 women aged 35 years and older and the control group - 325 women under 35 years. Additionally, in the main group there were 2 subgroups: 1st - 199 women aged 35-39 years, 2nd - 124 women over 40 years. Statistical processing of the results was performed by methods of variation statistics adopted in biology and medicine. Indicators are presented as the absolute number of cases in the group and the frequency in percent - n (%). Differences between samples by indicators were made using Fisher's exact test. The significance level  $p = 0.05$  was considered critical.

Research results and their discussion. Statistical calculation allowed to establish the distribution of patients by age according to the years of the study, which is presented in table 1. As we can see, the lowest share is expected to be made by patients under 25 (from 2.4% in 2015 to 3.3% in 2018 and 2.6% in 2019, on average 3.0%). The largest share in 2015 - 2017 were women aged 30-34 years (from 32.0% to 30.7%), but since 2018 the first place in the distribution was taken by a group of patients aged 35-39 years. (30.7% and 32.1% respectively). There is a gradual annual trend of increasing the share of the oldest age group over 40 years (from 18.3% in 2015 to 21.6% in 2019), and the total share of such patients is quite significant (average for 5 years 20.4 %, which is even higher than patients under 30 years - 18.5%). If you take the border to accept In recent years, intraplasmic sperm injection (ICSI) has been most frequently used among ART methods in both the main and control groups: 42.2% in the main group and 47.7% in the control group ( $p > 0.05$ ), with the share of women in

the oldest age group was significantly lower than in the control (38.7%,  $p < 0.05$ ). In second place in terms of frequency of use - transfer of cryopreserved embryos (41.5% and 43.7% in the main and control groups,  $p > 0.05$ ), groups from 35 to 40 years and after 40 years also did not differ in this indicator. Older women were significantly more likely to use oocyte donation (OC) compared to the control group (14.2% vs. 3.7%, respectively,  $p < 0.05$ ). In group 2 K used almost a quarter of patients, which is significantly higher than in group 1 (23.4% vs. 8.5%,  $p < 0.05$ ), due to age-related decline in ovarian reserve. *In vitro* fertilization (IVF) without ICSI has been used quite rarely in all groups of patients, as have sperm biopsy methods.

The data characterizing the features of infertility by groups of patients are shown in table 3. The analysis revealed a significant discrepancy in the distribution of the etiology of infertility: if in the control the largest share was a combination of factors (31.1%) and tubal factor (25.2%), in older women, half (48.0% vs. 17.2% in the control,  $p < 0.05$ ) of women are classified in the subgroup "only another female factor", which includes endocrinological disorders, ovarian insufficiency and others. In group 2 (over 40 years) there were 57.3% against 42.2% of patients aged 35 to 40 years ( $p < 0.05$ ). It is noteworthy that in the main group there are significantly fewer patients diagnosed with only the male factor (8.0% vs. 20.9% in the control group,  $p < 0.05$ ). By the age of 35, half of the cases have primary infertility, while in the main group only one third (34.1% vs. 48.0%, respectively,  $p < 0.05$ ), in group 2 such women are also significantly less than in group 1 (27.4% vs. 38.2%,  $p < 0.05$ ).

Half of the women in the main group of infertility lasted more than 5 years (50.0% vs. 30.2% of women in the control group,  $p < 0.05$ ), in group 2 such women were 55.6% vs. 46.7% - in group 1 ( $p > 0.05$ ). Decreased ovarian reserve by ultrasound and hormonal parameters was diagnosed in 48.0% of patients in the main group, which is significantly higher than in the control group (16.0%,  $p < 0.05$ ), the highest percentage of such women is expected in group 2 (57.3 % against 42.2%,  $p < 0.05$ ), which corresponds to the indicators of FSH increase and decrease in AMG relative to age norms (see Table 3.3). A quarter of women in the main group already had one failed IVF attempt in the anamnesis (24.0% vs. 18.5% in the control group,  $p < 0.05$ ), and 12.6% - 2 or more attempts (vs. 8.0% in control,  $p < 0.05$ ). In group 2, the highest proportion of women with at least two IVF attempts (16.9% vs. 10.1% in group 1,  $p < 0.05$ ). The figure shows the results of the success of this cycle of IVF in terms of clinical pregnancies and live births for the started cycle.

Significantly worse results were obtained in the main group: 30.0% of clinical pregnancies (against 39.1% in the control group,  $p < 0.05$ ) and 21.1% of live births (against 30.2%, respectively,  $p < 0.05$ ). In group 2, the worst results were obtained both for the control group and for group 1 (only 21.8% vs. 35.2% in group 1 for clinical pregnancies and 13.7% vs. 25.6% for live births,  $p < 0.05$ ).

in both cases), while the indicators of group 1, although they tend to decrease relative to the control group, but the difference is not significant ( $p > 0,05$ ).

## Conclusion

More than half (50.6%) of ART patients are women of older reproductive age (after 35 years), and almost 40% (39.0%) of them are older than 40 years. There is a tendency to a gradual increase in the share of older women who want to become mothers: in 2019 the share of women aged 35 and over increased by 6.1% compared to 2015 (from 47.6% to 53.7%), which corresponds to the global trend of "deferred motherhood". Women - patients of ART programs of the older age group were much more often forced to use oocyte donation (14.2% vs. 3.7% under 35 years). After 40 years, this method of ART was used by almost a quarter of patients (23.4%).

Due to infertility, half of 48.0% of older women are classified in the subgroup "only another female factor", which includes endocrinological disorders, ovarian failure and others. After 35 and 40 years, the share of women with primary infertility decreases (34.1% and 27.4% against 48.0% before the age of 35) and the share of those who suffer from infertility for more than 5 years increases. Decreased ovarian reserve was diagnosed in 48.0% of patients after 35 years, after 40 years this figure reaches 57.3%, which corresponds to the indicators of increased FSH and decreased AMG relative to age.

A quarter (24.0%) of women after the age of 35 already had one failed IVF attempt in the anamnesis, and 12.6% - 2 or more attempts. After 40 years, the proportion of women with at least two IVF attempts increases to 16.9%. After 35 years, the share of clinical pregnancies per started cycle (30.0% vs. 39.1%) and live births (21.1% vs. 30.2%) significantly decreases. After 40 years, these 2 indicators fall sharply and are 21.8% and 13.7%.

Given the increasing proportion of women who resort to ART in older reproductive age, as well as a number of factors that worsen the prognosis of ART, among which the reduction of ovarian

reserve is the least controlled, it is important to find methods to optimize approaches to training patients of late reproductive age. quality mature oocytes.

## References

1. Aghajanova L, Hoffman J, Mok-Lin E, Herndon CN (2017) Obstetrics and Gynecology Residency and Fertility Needs. *Reprod Sci* 24(3): 428-434.
2. Faddy MJ, Gosden MD, Gosden RG (2018) A demographic projection of the contribution of assisted reproductive technologies to world population growth. *Reprod Biomed Online* 36(4): 455-458.
3. Pisarska MD, Chan JL, Lawrenson K, Gonzalez TL, Wang ET, et al. (2019) Genetics and Epigenetics of Infertility and Treatments on Outcomes. *J Clin Endocrinol Metab* 104(6): 1871-1886.
4. Jackson S, Hong C, Wang ET, Alexander C, Gregory KD, et al. (2015) Pregnancy outcomes in very advanced maternal age pregnancies: the impact of assisted reproductive technology. *Fertil Steril* 103(1): 76-80.
5. Wang ETRL, Ramos L, Vyas N, Bhasin G, Simmons CF, et al. (2018) Maternal and neonatal outcomes associated with infertility. *J Matern Fetal Neonatal Med* 20: 1-4.
6. Zabolotko VM (2019) Information and statistical reference book on assisted reproductive technologies in Ukraine. Kyiv: Dz "Center for Medical Statistics of the Ministry of Health of Ukraine", 2019.
7. Wasilewski T, Łukaszewicz-Zajac M, Wasilewska J, Mroczko B (2020) Biochemistry of infertility. *Clin Chim Acta* 508: 185-190.
8. Schmidt L, Sobotka T, Bentzen JG, Nyboe AA (2012) ESHRE Reproduction and Force Society Task. Demographic and medical consequences of the postponement of parenthood. *Hum Reprod Update* 18: 29-43.
9. <https://www12.statcan.gc.ca/census-recensement/index-eng.cfm?MM=1>
10. Eurostat (2015) Women in the EU gave birth to their first child at almost 29 years of age on average 2015.
11. Cimadomo D, Fabozzi G, Vaiarelli A, Ubaldi N, Ubaldi FM, et al. (2018) Impact of maternal age on oocyte and embryo competence. *Front Endocrinol* 9: 327.
12. Wyndham N, Marin Figueira PG, Patrizio P (2012) A persistent misperception: assisted reproductive technology can reverse the "aged biological clock". *Fertil Steril* 97(5): 1044-1047.
13. (2014) Prevention CfDca.



This work is licensed under Creative Commons Attribution 4.0 License  
DOI: [10.19080/JGWH.2022.21.556089](https://doi.org/10.19080/JGWH.2022.21.556089)

### Your next submission with Juniper Publishers will reach you the below assets

- Quality Editorial service
- Swift Peer Review
- Reprints availability
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats  
( Pdf, E-pub, Full Ttext, Audio )
- Unceasing customer service

Track the below URL for one-step submission  
<https://juniperpublishers.com/online-submission.php>