

RETROSPECTIVE ANALYSIS OF REPRODUCTIVE FUNCTION IN WOMEN OF LATE REPRODUCTIVE AGE

Khurshida Z. Akhmedzhanova¹, Farkhad I. Shukurov²

¹ Assistant of the Department of Obstetrics and Gynecology at the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: xurshidazakirovna@mail.ru

² Head of the Department of Obstetrics and Gynecology at the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: prof.farxadshukurov@gmail.com

ABSTRACT

Aim. To conduct a retrospective analysis of the reproductive function status in women of late reproductive age, assess ovarian reserve and hormonal status, and identify factors that may affect this function.

Materials and methods. The study included 100 women aged 36 to 43 with late reproductive age, whose reproductive function status was examined based on their medical records stored in the archive of the Interdistrict Perinatal Center No. 9 in Tashkent city. Among them, 50 women aged 36-40 years were assigned to Group I, and 50 women aged 41-43 years were included in Group II. Data were collected for each patient on age, ethnicity, lifestyle, diseases, and reproductive history.

Results. Various menstrual cycle disorders were identified in 70% of women participating in the study, including amenorrhea in 25%, oligomenorrhea in 30%, and abnormal uterine bleeding in 15%. Ovulatory problems were diagnosed in 30% of women. Reproductive function issues were found in 74.3% of women, with primary infertility observed in 40% of cases and secondary infertility in 60%.

Conclusion. The results of the retrospective analysis of reproductive function in women of late reproductive age showed that 85% of them had significant reproductive dysfunction, 70% had various menstrual cycle disorders, 60% had anovulatory conditions, and 55% experienced hormonal imbalances. These problems are often associated with age, prior pelvic surgeries, and chronic diseases, negatively impacting reproductive function. The study results highlight the need for accurate ovarian reserve assessment and development of individualized treatment plans.

Key words: retrospective analysis, reproductive function, women of late reproductive age.

INTRODUCTION

The decline in reproductive function among women of late reproductive age is an urgent issue requiring serious attention and research [1-5]. In today's world, many women are delaying childbearing for various reasons, including career aspirations, financial stability, and personal circumstances [6-11]. However, increasing age, especially after 35, significantly reduces the likelihood of conception and increases the risk of reproductive challenges [12-17]. According to the World Health Organization (WHO), 10-15% of women aged 35-40 experience difficulties with conception, and this rate rises to 30-40% by age 45 [18-23]. Age-related fertility decline is also associated with factors such as diminished ovarian reserve, hormonal imbalances, and a higher risk of gynecological conditions like endometriosis and fibroids [24-26]. A 2023 study by Harris B.S. et al. indicated that women over 35 face a significantly higher risk of infertility than younger women due to the decrease in both quantity and quality of oocytes [27]. This issue is particularly relevant for families planning pregnancies and for medical professionals involved in the treatment and restoration of reproductive function [28-30]. Given the importance of this issue and the global trends toward delayed motherhood, this study aims to conduct a retrospective analysis of reproductive function in women of late reproductive age and identify factors that may influence it.

Aim of the study to conduct a retrospective analysis of the reproductive function status in women of late reproductive age by assessing ovarian reserve and hormonal status, as well as identifying factors that may influence these functions.

Materials and methods.

This study involved a retrospective analysis of the reproductive function status of 100 women of late reproductive age (36–43 years) who were under observation at the family polyclinic of the Tashkent City Interdistrict Perinatal Center No. 9 from 2021 to 2022. The medical records of these women, stored at the center, were reviewed. Participants were divided into two groups: Group I included 50 women aged 36-40 years, and Group II included 50 women aged 41-43 years. The study was conducted in a retrospective design. For each patient, the following information was collected: age, heredity, lifestyle, presence of diseases, reproductive history, and history of abdominal and pelvic surgeries.

The assessment of reproductive function included the analysis of hormonal profiles (estrogens, progesterone, gonadotropic hormone levels), ultrasound examination of pelvic organs and mammary glands, mammography, and polymerase chain reaction (PCR) tests for chlamydia and herpes detection.

Additionally, the study examined the relationship between contraceptive use and reproductive function status in each group.

Data were processed using the Epi Info 7.2.2.2 statistical software. Spearman correlation analysis was performed using the STATISTICA 10.0 software package to identify correlations between variables. Differences with $p < 0.05$, $p < 0.01$, and $p < 0.001$ were considered statistically significant.

Results.

The average age of the participants was 39.5 ± 0.28 years. A retrospective analysis of reproductive function in 100 women of late reproductive age provided significant insights into factors impacting reproductive health. Primary infertility was identified in 40 women (40%), while secondary infertility was found in 60 women (60%). Among the 100 participants, 60% had higher education, while 40% had secondary education. Additionally, 70% of the women were employed, and 30% were homemakers.

Chronic conditions were observed in 40 participants (40%), including diabetes in 20%, hypertension in 15%, and cardiovascular diseases in 10%. Among the participants, 20% had a history of abdominal surgeries, such as appendectomy and cholecystectomy, while 15% had undergone laparoscopic surgeries for ovarian cysts, cystic changes, and tubal pathologies.

Data collected for each woman included reproductive history, heredity, lifestyle, presence of diseases, and records of previous conservative and surgical interventions. Hormonal assessments, ultrasound evaluations of pelvic organs and mammary glands, and PCR tests for chlamydia and herpes were conducted on all participants.

Hormonal analysis revealed that estradiol levels were below normal in 65% of the women, with an average estradiol range of 25-35 pg/ml, indicating diminished reproductive function. In anovulatory women, progesterone levels were below 3-4 ng/ml, signifying absent or low ovulatory activity; this was observed in 45% of participants. Luteinizing hormone (LH) levels were above normal in 70% of women, averaging 20-25 mIU/ml, reflecting reduced ovarian function and diminished ovulatory processes in women of late reproductive age. Additionally, follicle-stimulating hormone (FSH) levels were above normal in the majority of participants, with levels ranging from 15-20 mIU/ml, indicating diminished ovarian reserve in 60% of women.

Ultrasound findings of the pelvic organs revealed a reduction in follicle count in 75% of women, with some having fewer than five follicles. Fibrotic and cystic changes in ovarian tissue were identified in 50% of the participants. Furthermore, endometrial hyperplasia was observed in 30% of women, with endometrial

thickness ranging from 7-8 mm on ultrasound, which was associated with ovulatory dysfunction. Anatomical changes in the fallopian tubes were found in 20% of women, potentially hindering pregnancy.

Mammary gland ultrasound and mammography findings revealed fibroadenomas and small cysts (3-5 mm in diameter) in 40% of women, which, while generally benign, require periodic monitoring.

Polymerase chain reaction (PCHR) testing identified chlamydia infection in 30% of women, increasing the risk of pelvic inflammation and fallopian tube damage. Additionally, herpes virus was detected in 20% of participants, which may negatively affect ovulation and tubal patency.

The findings among these women of late reproductive age indicated hormonal imbalance, reduced ovarian function, structural changes in the ovaries, and the presence of infections. These factors contribute to diminished reproductive function, underscoring the need for individualized treatment and preventive care plans to improve reproductive health.

In total, 70 of the 100 women (70%) had various menstrual cycle disorders, including amenorrhea in 25%, oligomenorrhea in 30%, abnormal uterine bleeding in 15%, and anovulatory issues in 30% (see Figure 1).

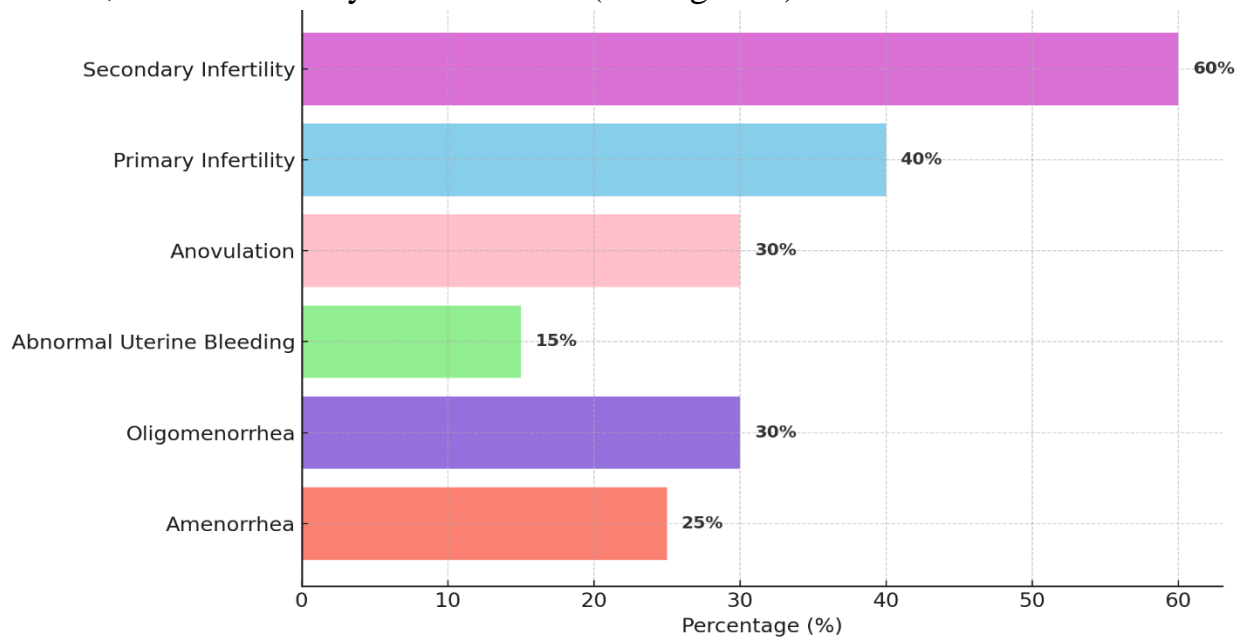


Figure 1. Analysis Results of Reproductive Function in Women of Late Reproductive Age, %

The study found that 74.3% of women had issues related to reproductive function. Primary infertility was recorded in 40% of women, while secondary infertility was observed in 60%.

The study identified several risk factors contributing to reproductive function disorders, including: age over 35 years (RR=1.4; OR=1.8), presence of chronic gynecological diseases (RR=1.6; OR=1.9), history of ovarian surgeries (RR=1.7; OR=2.1), surgical interventions on the uterus and fallopian tubes (RR=1.5; OR=1.8), and inflammatory diseases of the ovaries and fallopian tubes (RR=1.4; OR=1.7).

Based on the study results, the following treatments were applied to women: hormonal therapy — 37.0%, surgeries for cyst and fibroid removal — 15%, ovulation induction — 30%, and antibacterial therapy — 18.0%.

Retrospective analyses indicate a need for in-depth studies of reproductive function disorders in women of late reproductive age, as well as the development of individualized intervention plans. Emphasis should be placed on innovative diagnostic and treatment methods to optimize fertility.

Discussion.

The findings of this study highlight several significant factors contributing to the decline in reproductive function among women of late reproductive age (36-43 years). The data underscore the complex interplay between age, hormonal imbalances, structural changes, and infections that collectively impact fertility in this demographic. This discussion will explore these factors in greater detail and assess their implications for clinical practice.

One of the primary issues observed was the substantial hormonal imbalance affecting the participants. Estradiol levels were below normal in 65% of the women, indicative of diminished ovarian function, which aligns with findings from previous studies demonstrating a decline in ovarian reserve and hormonal function as age advances. Furthermore, the elevated luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels in a majority of participants signify a reduced ovarian reserve and compromised ovulatory function, consistent with other studies on age-related reproductive decline. These hormonal shifts exacerbate reproductive challenges, as low estradiol and progesterone levels reduce the likelihood of successful ovulation and pregnancy.

The structural changes identified via ultrasound further support the association between age and reproductive decline. Reduced follicle count, fibrotic changes, and cystic formations were observed in a significant portion of the participants, with 75% showing a reduction in follicle count and 50% displaying fibrotic or cystic changes in ovarian tissue. Such alterations are consistent with age-related fibrosis and cyst formation in ovarian tissue, which negatively affect fertility potential. Additionally, endometrial hyperplasia, observed in 30% of women, suggests that ovulatory dysfunction further contributes to fertility

challenges by affecting endometrial receptivity. The anatomical changes in the fallopian tubes found in 20% of participants highlight another significant obstacle to conception, as tubal pathologies can impede the fertilization process.

The presence of infections, including chlamydia (30%) and herpes (20%), adds another layer of complexity to reproductive health in this group. Chlamydia infection, a known risk factor for pelvic inflammatory disease, can cause damage to the fallopian tubes, while herpes virus infections can disrupt normal ovulatory cycles and potentially reduce tubal patency. These infections underscore the importance of regular screenings for sexually transmitted infections, particularly for women at an advanced reproductive age, as untreated infections can compound existing reproductive issues.

The prevalence of menstrual cycle disorders among the participants is notable, with 70% reporting various abnormalities, including amenorrhea, oligomenorrhea, abnormal uterine bleeding, and anovulatory cycles. These findings reflect the high incidence of cycle irregularities that typically accompany reproductive aging and underscore the need for targeted interventions to manage menstrual health in older women aiming to conceive.

The study also identified key risk factors that exacerbate reproductive function disorders, such as age over 35, chronic gynecological diseases, a history of ovarian and uterine surgeries, and inflammatory diseases of the ovaries and fallopian tubes. These risk factors align with established literature, which recognizes that advancing age and previous surgeries can compromise ovarian and uterine function, while inflammation from chronic infections further disrupts fertility.

The treatment approaches implemented, including hormonal therapy (37%), ovulation induction (30%), and surgeries for cyst and fibroid removal (15%), illustrate the necessity of a multifaceted approach to address these complex issues. While hormonal therapy can help balance deficiencies and support ovarian function, ovulation induction directly targets anovulatory challenges. Additionally, antibacterial therapy (18%) is crucial for managing infections and reducing the risk of further pelvic inflammatory diseases.

These findings collectively point to the need for individualized and comprehensive treatment plans tailored to the unique hormonal, structural, and infectious profiles of each patient. Furthermore, they underscore the importance of early intervention, especially for women over 35 who are planning pregnancies, as proactive management of reproductive health could mitigate age-related decline.

This study's retrospective approach provides valuable insights but also highlights the need for further prospective studies to explore innovative diagnostic and treatment methods. Given the rapid advancements in reproductive medicine,

integrating novel technologies, such as fertility-preserving surgical techniques, advanced hormonal therapies, and personalized treatment protocols, may enhance fertility outcomes in this population.

In conclusion, age-related reproductive decline in women of late reproductive age is a multifaceted issue that requires a thorough understanding of hormonal, structural, and infectious factors. Implementing personalized, evidence-based treatment strategies can improve reproductive health and optimize fertility outcomes in this growing demographic. Further research focused on innovative and individualized interventions is warranted to address the unique challenges facing women of late reproductive age seeking to conceive.

Conclusion. According to the results of the retrospective analysis conducted in women of late reproductive age, serious reproductive function disorders were identified in 85% of cases, with 70% presenting various menstrual irregularities, 60% showing anovulatory conditions, and 55% exhibiting hormonal imbalance. These issues are often associated with age, previous uterine surgeries, and chronic illnesses, which negatively impact reproductive function. The study underscores the necessity for accurate assessment of ovarian reserve and the development of individualized treatment plans.

REFERENCES

1. Aftabsavad S, Noormohammadi Z, Moini A, Karimipoor M. Effect of bisphenol A on alterations of ICAM-1 and HLA-G genes expression and DNA methylation profiles in cumulus cells of infertile women with poor response to ovarian stimulation. *Sci Rep.* 2021 May 5;11(1):9595. doi: 10.1038/s41598-021-87175-1.
2. Au LS, Feng Q, Shingshetty L, Maheshwari A, Mol BW. Evaluating prognosis in unexplained infertility. *Fertil Steril.* 2024 May;121(5):717-729. doi: 10.1016/j.fertnstert.2024.02.044.
3. Cabry R, Merviyel P, Hazout A, Belloc S, Dalleac A, Copin H, Benkhalifa M. Management of infertility in women over 40. *Maturitas.* 2014 May;78(1):17-21. doi: 10.1016/j.maturitas.2014.02.014.
4. Cao Y, Zhao X, Dou Z, Gong Z, Wang B, Xia T. The correlation between menstrual characteristics and fertility in women of reproductive age: a systematic review and meta-analysis. *Fertil Steril.* 2024 Jun 25(24):00547-8. doi: 10.1016/j.fertnstert.2024.06.016.
5. Harris BS, Jukic AM, Truong T, Nagle CT, Erkanli A, Steiner AZ. Markers of ovarian reserve as predictors of future fertility. *Fertil Steril.* 2023 Jan;119(1):99-106. doi: 10.1016/j.fertnstert.2022.10.014.

6. He YJ, Yi DN, Cai CF, Zhu CY, Zhan WT, Chen L. Serum anti-Mullerian hormone level and its predictive value for pregnancy outcomes in women of late reproductive age. *J Biol Regul Homeost Agents*. 2020 Nov-Dec;34(6):2153-2157. doi: 10.23812/20-364-L.
7. Hosseinisadat R, Farsi Nejad A, Mohammadi F. Intra-ovarian infusion of autologous platelet-rich plasma in women with poor ovarian reserve: A before and after study. *Eur J Obstet Gynecol Reprod Biol*. 2023 Jan;280:60-63. doi: 10.1016/j.ejogrb.2022.11.001.
8. Jabchenko I. A., Syudmak O. R. Osobennosti fertilitnosti u jenshin starshego reproduktivnogo vozrasta: problemy otlojennogo detorojdeniya i metody ix korreksii. *Reproduktivnaya meditsina*. 2019;3(40):29-36.
9. Jeleznaya A. A., Myagkix I. I. Preodoleniye besplodiya u jenshin v pozdnem reproduktivnom vozraste so snijennym ovarialnym rezervom. *Mediko-sotsialnye problemy semi*. 2021;26(3):39-45.
10. Kang JH, Kim YS, Lee SH. Comparison of hemostatic sealants on ovarian reserve during laparoscopic ovarian cystectomy. *Eur J Obstet Gynecol Reprod Biol*. 2015;94:64-67.
11. Kawamura K, Sato Y. Effectiveness of supplement ingredients on infertility treatment in advanced aged women. *J Obstet Gynaecol Res*. 2023 Aug;49(8):2015-2022. doi: 10.1111/jog.15683. Epub 2023 May 21.
12. Kim C, Slaughter JC, Terry JG, Jacobs DR Jr, Parikh N, Appiah D, Leader B, Moravek MB, Wellons MF. Antimüllerian hormone and F2-isoprostanes in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Fertil Steril*. 2020 Sep;114(3):646-652. doi: 10.1016/j.fertnstert.2020.04.028.
13. Korolkova A. I., i dr. Antimiyullerov gormon kak pokazatel fertilitnosti jenshin pozdnego reproduktivnogo vozrasta. *Problemy reproduksii*. 2018;24(2):23-27.
14. Kus Ye. Ye., i dr. Jenskoye besplodiye. *FORCIPE*. 2021;4(S1):107-107.
15. Li Q, Zhao L, Zeng Y, Kuang Y, Guan Y, Chen B, Xu S, Tang B, Wu L, Mao X, Sun X, Shi J, Xu P, Diao F, Xue S, Bao S, Meng Q, Yuan P, Wang W, Ma N, Song D, Xu B, Dong J, Mu J, Zhang Z, Fan H, Gu H, Li Q, He L, Jin L, Wang L, Sang Q. Large-scale analysis of de novo mutations identifies risk genes for female infertility characterized by oocyte and early embryo defects. *Genome Biol*. 2023 Apr;24(1):68. doi: 10.1186/s13059-023-02894-0.
16. Lizneva D. The criteria, prevalence and phenotypes of PCOS. *Fertil Steril*. 2016;106(6):15-35.
17. Macut D, Bjekić-Macut J, Rahelić D, Doknić M. Insulin and the polycystic ovary syndrome. *Diabetes Res Clin Pract*. 2017;130:163–170.

18. Meczekalski B, Czyzyk A, Kunicki M, Podfigurna-Stopa A, Plociennik L, Jakiel G, Maciejewska-Jeske M, Lukaszuk K. Fertility in women of late reproductive age: the role of serum anti-Müllerian hormone (AMH) levels in its assessment. *J Endocrinol Invest.* 2016 Nov;39(11):1259-1265. doi: 10.1007/s40618-016-0497-6. Epub 2016 Jun 14.
19. Moolhuijsen LME, Visser JA. Anti-Müllerian Hormone and Ovarian Reserve: Update on Assessing Ovarian Function. *J Clin Endocrinol Metab.* 2020 Nov 1;105(11):3361–73. doi: 10.1210/clinem/dgaa513.
20. Nazarenko T. A. Stimulyatsiya funktsii yaichnikov. Moskva: MEDpress-inform; 2023. 268 s.
21. Nunes ACV, Trevisan CM, Peluso C, Loureiro FA, Dias AT, Rincon D, Fonseca FLA, Christofolini DM, Laganà AS, Montagna E, Barbosa CP, Bianco B. Low and High-Normal FMR1 Triplet Cytosine, Guanine Guanine Repeats Affect Ovarian Reserve and Fertility in Women Who Underwent In Vitro Fertilization Treatment? Results from a Cross-Sectional Study. *DNA Cell Biol.* 2024 Aug;43(8):414-424. doi: 10.1089/dna.2023.0395.
22. Shukurov F.I., Ayupova F.M. Rol adyuvantnoy gormonalnoy terapii v vosstanovlenii reproduktivnoy funktsii u jenshin posle endoxirurgicheskogo lecheniya follikulyarnyx kist yaichnikov. *Ginekologiya*, vol. 23, no. 1, 2021, pp. 68-72.
23. Shukurov F.I. Minimally Invasive Surgery in Restoring Reproductive Function of Female Infertility Caused by Benign Ovarian Structural Changes. *American Journal of Medicine and Medical Sciencies* 2016, 6(6): 182-185 DOI: 10.5923/j.ajmms.20160606.04.
24. Shukurov, F. I. The results of immunohistochemical studies of the endometrial receptors in women with infertility caused by benign ovarian structural changes. 7th International IVI Congress” held in Bilbao (Spain). Vol. 1. 2017.
25. Shukurov F. I. et al. Otsenka effektivnosti primeneniya preparata “Belara” v adyuvantnoy terapii sindroma polikistoznix yaichnikov posle endoxirurgicheskogo lecheniya //Eksperimentalnaya i klinicheskaya farmakologiya. – 2022. – T. 85. – №. 8. – S. 14-16.
26. Shukurov, F. I. Yordamchi reproduktiv texnologiyalar. (2024).
27. Shukurov F. I., Ayupova F. M., Korolkova A. I. et al. Antimyullerov gormon kak pokazatel fertlnosti jenshin pozdnego reproduktivnogo vozrasta. *Problemy reproduksii.* 2018;24(2):23-27.
28. Kus Ye. Ye., Korolkova A. I., i dr. Jenskoye besplodiye. *FORCIPE.* 2021;4(S1):107-107.

29. Li Q, Zhao L, Zeng Y, Kuang Y, Guan Y, Chen B, Xu S, Tang B, Wu L, Mao X, Sun X, Shi J, Xu P, Diao F, Xue S, Bao S, Meng Q, Yuan P, Wang W, Ma N, Song D, Xu B, Dong J, Mu J, Zhang Z, Fan H, Gu H, Li Q, He L, Jin L, Wang L, Sang Q. Large-scale analysis of de novo mutations identifies risk genes for female infertility characterized by oocyte and early embryo defects. *Genome Biol.* 2023Apr6;24(1):68. doi: 10.1186/s13059-023-02894-0.

30. Lizneva D. The criteria, prevalence and phenotypes of PCOS. *Fertil Steril.* 2016;106(6):15-35.