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# Improving Diagnostic and Therapeutic Measures in in Vitro Fertilization Cycles Based on Homocysteine Levels

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**Abstract:** This study explores the impact of homocysteine levels on infertility and IVF outcomes. A total of 50 patients with abnormal homocysteine levels underwent IVF after normalization, while 40 patients proceeded without prior testing. The results showed a significant improvement in antral follicle count (16.15±1.45 vs. 12.76±1.28, $p<0.05$) and high-quality oocyte retrieval (9.25±0.87 vs. 8.00±1.26, $p<0.05$) in the main group. Pregnancy rates were also higher in the main group (62% vs. 47.5%, OR=1.8, $p<0.05$). These findings suggest that optimizing homocysteine levels before IVF can enhance pregnancy success rates by up to 14%.

**Keywords:** infertility, homocysteine, IVF protocol, transvaginal puncture, embryo, IVF pregnancy.

## I. Introduction

Infertility prevalence and the role of assisted reproductive technologies

Infertility affects between 8% and 20% of couples, with more than half of infertility cases resulting from reproductive disorders in women [Sukhikh G.T. et al., 2020; Krasnopolskaya K.V., Nazarenko T.A., 2013]. Globally, approximately 15% of reproductive-age couples experience infertility, and this figure has remained stable. The advent and development of assisted reproductive technologies (ART) have marked a new era in infertility treatment, offering novel opportunities to explore the pathogenetic, morphological, embryological, and cytogenetic aspects of reproduction.

In vitro fertilization (IVF) has become one of the most widely used and effective ART methods worldwide, including in Uzbekistan, for treating infertility. A review of Uzbek scientific literature on ART, its effectiveness, innovations, and ongoing research indicates that 20% of women aged 35–44 require IVF services. However, as women age, the number of ovarian follicles declines significantly—from 7 million at birth to only 25,000 by the end of age 37—often leading to the formation of aneuploid embryos in later reproductive years. The frequency of aneuploidy is strongly correlated with maternal age, being 5% higher in women aged 30–35 compared to those aged 24–29, with this gap progressively increasing over time.

Additionally, spontaneous abortion rates due to fetal trisomy are 15% at age 25, rise to 33% at ages 30–35, and exceed 65% after age 40. In IVF cycles, aneuploidy is linked to low fertilization rates, impaired embryo implantation, slow embryonic development, and reduced pregnancy success rates. Regardless of embryo morphology, aneuploidy frequency increases with maternal age, with post-meiotic chromosomal abnormalities being particularly prevalent. These findings highlight the necessity of optimizing ovarian stimulation protocols in IVF for women of reproductive age (M.M. Maksudova, 2024).

Furthermore, scientific literature suggests that inhibins and activins are multifunctional hormones belonging to the growth factor family, playing a crucial role in regulating follicle-stimulating hormone (FSH) synthesis and secretion (L.A. Lifshits, S.A. Kravchenko, Genetic Aspects of Premature Ovarian Failure). Their synthesis occurs in granulosa cells during the early stages of follicular development. Researchers propose that inhibins primarily regulate FSH secretion in women, with serum inhibin concentration decreasing as ovarian follicle reserves decline. Meanwhile, increasing FSH concentrations correspond with follicular depletion and the transition to menopause.

Correlation Between Homocysteine Levels, Embryo Quality, and Oocyte Quality. Numerous potential correlations have been identified between homocysteine levels and the quality of embryos and oocytes. In particular, scientific literature extensively discusses the direct correlation between homocysteine levels and the quality of oocytes and embryos in couples suffering from infertility associated with polycystic ovary syndrome (PCOS) (Wang F. et al., 2019).

Hyperhomocysteinemia, characterized by elevated homocysteine levels in the blood during reproductive age, has been recognized in multiple studies as a risk factor in cases of unexplained infertility (Razi Y. et al., 2021; Berker B. et al., 2009). In women of advanced reproductive age, increased plasma homocysteine levels in IVF protocols have been linked to the activation of thrombotic factors, which in turn reduce the success rates of IVF outcomes (Grandone E. et al., 2004). Furthermore, elevated homocysteine levels may contribute to implantation failures during the final stage of IVF—embryo transfer—potentially leading to poor IVF success rates and persistent infertility (Agrawal A. et al., 2015).

Some studies suggest that successful embryo transfer in IVF is more frequently observed in couples with normal homocysteine levels (Nufar F. et al., 2023), emphasizing the need for a multi-factorial scientific approach to addressing this issue. Additionally, another study indicates an inverse correlation between estradiol levels—elevated due to ovarian stimulation in IVF protocols—and homocysteine concentrations in the blood (Lox D. et al., 2000).

## II. Aim of the work

To determine the role of elevated or reduced homocysteine levels in infertility and to improve the quality of embryos and oocytes, as well as pregnancy outcomes and its progression in IVF cycles, by optimizing diagnostic and therapeutic approaches aimed at correcting homocysteine levels.

## III. Materials and methods

Scientific Study on Homocysteine Levels in IVF Patients at “Siz Ona Bo‘lasiz” Center (2022-2025). This scientific study was conducted between 2022 and 2025 at the “Siz Ona Bo‘lasiz” IVF Center. The study included 90 women, who were divided into two groups. The main group consisted of 50 patients who underwent IVF protocols with homocysteine levels maintained within the 5-8 μmol/L range. The control group comprised patients who also underwent IVF protocols but did not have their homocysteine levels monitored.

During the study, a dedicated medical record was created for each participant, documenting anamnesis, general and gynecological examination results, and laboratory diagnostic findings. Homocysteine levels were measured both before the IVF protocol and after treatment.

The study focused on analyzing the correlation between homocysteine levels and key reproductive indicators, including:

- Type and duration of infertility
- Type and duration of ovarian stimulation medication
- Number of oocytes retrieved during follicular puncture (including M2 and 2Pn stage oocytes)
- Number of embryos, number of fully developed embryos
- Presence or absence of male factor infertility

All participants in the study underwent the same standardized IVF program, which included:

- Preparation for IVF
- Ovarian stimulation
- Transvaginal oocyte retrieval (puncture stage)
- Embryo transfer

All procedures were performed under identical conditions at the same IVF center and embryology laboratory to ensure methodological consistency. During the study, a dedicated medical record was created for each patient, which included:

- Anamnesis
- General and gynecological examination findings
- Laboratory diagnostic results

Homocysteine levels were measured before the initiation of the IVF protocol and after treatment in both subgroups of the main group.

The study analyzed the correlation of homocysteine levels with the following parameters:

- Patient age
- Duration of infertility
- Type and duration of ovarian stimulation medications
- Number of oocytes retrieved during puncture (including M2 and 2Pn-stage oocytes)
- Number of embryos and fully developed embryos
- Presence or absence of a male factor in infertility

The efficacy of the IVF protocol was evaluated based on the following criteria:

1. Biochemical pregnancy rate – Defined by serum β-hCG levels exceeding 20 mIU/mL.

2. Clinical pregnancy confirmation – Verified via ultrasound detection of a gestational sac in the uterus more than 20 days after embryo transfer.

This study provides crucial insights into the impact of homocysteine levels on IVF success rates and reproductive outcomes, highlighting the significance of pre-IVF homocysteine screening and management.

This comprehensive approach allowed for a deeper understanding of the impact of homocysteine levels on IVF success rates and reproductive outcomes.

**IV. Results**

An analysis of the age distribution among the study participants demonstrated that infertility and average age indicators were proportionally selected in both groups. The mean age in the main group and the control group was 31.3±3.8 years and 31.2±4.1 years, respectively (Table 1).

Table 1. Distribution of patients by AGE

| Age | Main group | | Control group | |
|---|---|---|---|---|
| | n-50 | % | n-40 | % |
| 20-34 | 41 | 86,0% | 30 | 75,0% |
| 35-44 | 9 | 14,0% | 10 | 25,0% |
| Mean age | 31,3±3.8 | | 31.2±4.1 | |

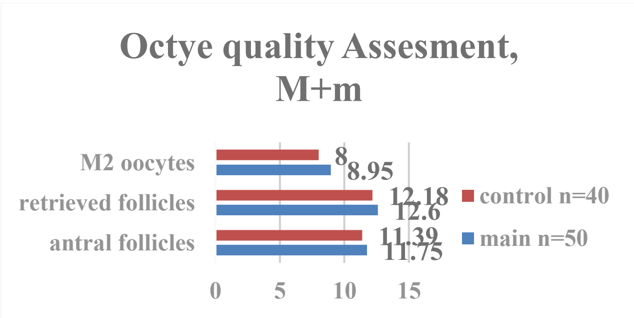
Analysis of Infertility Causes. During the examination, special attention was given to the infertility history of patients in both groups, with a particular focus on the distribution of homocysteine levels in relation to infertility causes. The study results confirmed that tubal factor infertility was the most common cause in both groups. Additionally, hormonal disorders were identified as the second most frequent cause, affecting 9 patients in the main group and 8 patients in the control group. Male factor infertility was detected in 10 cases in the main group and in the partners of 14 women in the control group.

A significant difference was observed between the groups in cases of unexplained infertility. In the main group, 16 women were diagnosed with unexplained infertility, whereas in the control group, this diagnosis was made in only 2 cases.

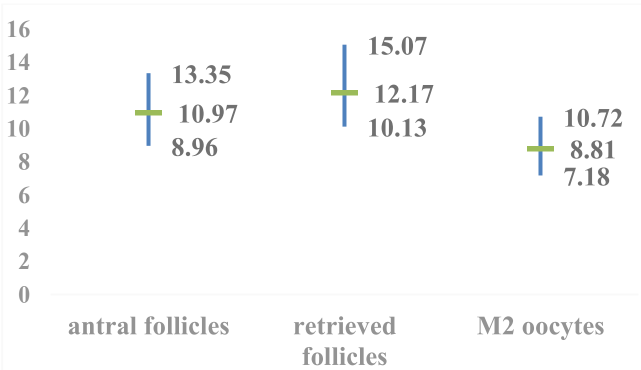
Oocyte Quality Assessment Results. In the main group, after ovarian stimulation in the IVF protocol and transvaginal puncture (TVP), the mean number of antral follicles, retrieved follicles, and M2 oocytes were 11.75±1.08, 12.6±1.22, and 8.95±1.01, respectively.

In the control group, these values were 11.39±1.35, 12.18±1.89, and 8.00±1.26, respectively ($p<0.05$), indicating a statistically significant difference in favor of the main group (Figure 1).

**Oocyte Quality Assessment Results, M+m**

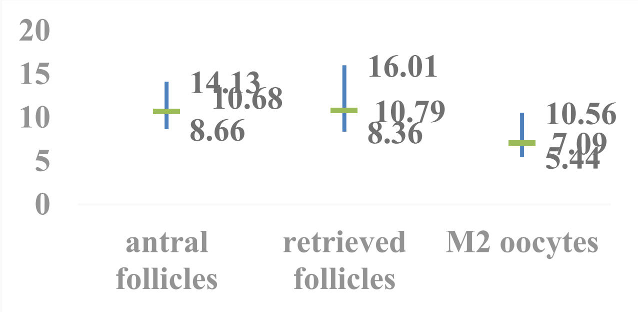



Correlation Analysis of Retrieved Oocytes in IVF Protocol. A comparative correlation analysis of oocytes retrieved during the IVF protocol in the main group demonstrated a statistically significant and reliable association ($p<0.05$) (Figure 2).




**A comparative correlation analysis (Main group)**

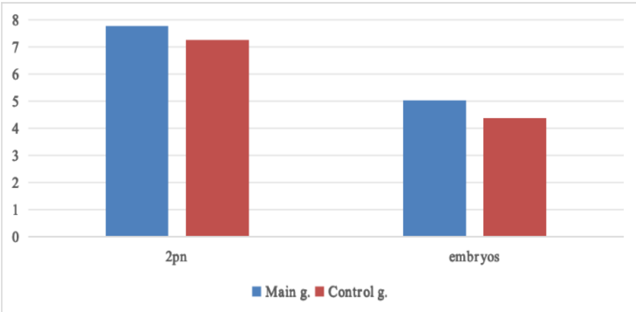
Similarly, in the control group, a correlation analysis of the retrieved oocytes confirmed a statistically significant relationship ($p<0.05$) (Figure 4).



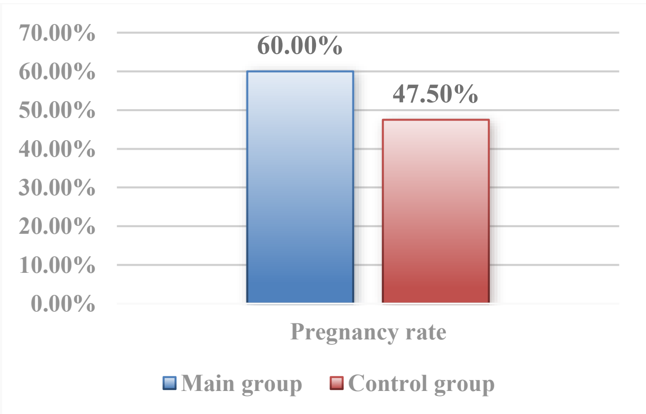

**A comparative correlation analysis (Control geoup)**

In terms of oocyte quality, the mean number of M2-stage oocytes in the main group was 8.95±0.87, while in the control group, it was 8.00±1.26 ($p<0.05$) (Figure 4).


A comparison of fertilization rates and embryo formation revealed significantly higher values in the main group compared to the control group. The 2PN fertilization rate was 7.78±0.80 in the main group versus 7.26±1.11 in the control group. The mean number of obtained embryos was 5.05±0.57 in the main group, compared to 4.37±0.57 in the control group (Figure 5).




Pregnancy Rate and Clinical Pregnancy Analysis. An analysis of pregnancy rates showed that in the control group, 19 out of 40 couples (47.5%) achieved pregnancy after a single embryo transfer in the first IVF cycle. In contrast, in the main group, where homocysteine levels were corrected before treatment, pregnancy was confirmed in 30 out of 50 couples (60.0%) after a single embryo transfer (Figure 6)



## Discussion

Abnormal homocysteine levels, whether elevated or reduced, have been identified as a significant factor in both primary and secondary infertility. Among patients in the main group, 60% were diagnosed with primary infertility, while 40% had secondary infertility. An analysis of infertility duration revealed that the average infertility duration in the main group was 5.7 ± 2.8 years, compared to 4.27 ± 1.9 years in the control group ($p<0.05$). These findings suggest that homocysteine dysregulation may contribute to prolonged infertility and a reduced likelihood of spontaneous conception.

Impact of homocysteine on male factor infertility. Regardless of the presence of a male factor in infertility, abnormal homocysteine levels were detected in both male and female partners. Semen analysis revealed that normal sperm parameters were observed in only 60.0% of male partners in the main group and 57.5% in the control group ($p<0.05$). These findings indicate that homocysteine may have a broader impact on reproductive function, potentially affecting both oocyte and sperm quality.

Homocysteine and oocyte quality in IVF cycles. The quantity and quality of retrieved oocytes were significantly influenced by homocysteine levels. Patients in the main group exhibited higher values for antral follicle count, retrieved follicles, and M2 oocytes (11.75±1.08, 12.6±1.22, and 8.95±1.01, respectively) compared to the control group (11.39±1.35, 12.18±1.89, and 8.00±1.26, $p<0.05$). Additionally, the mean number of high-quality M2 oocytes was higher in the main group (8.95±0.87) compared to the control group (8.00±1.26, $p<0.05$). These findings suggest that optimal homocysteine levels support improved follicular development and oocyte maturation, which are critical for IVF success.

Fertilization and embryo development. Maintaining homocysteine levels within the normal range was associated with higher fertilization rates and better embryo development. The 2PN fertilization rate in the main group was 7.78±0.80, compared to 7.26±1.11 in the control group. Similarly, the mean number of obtained embryos was 5.05±0.57 in the main group versus 4.37±0.57 in the control group ($p<0.05$). These results suggest a direct correlation between homocysteine regulation and improved embryonic development.

Pregnancy outcomes and IVF success rates. The study demonstrated that pre-IVF homocysteine normalization significantly improved pregnancy rates. In the control group, 47.5% (19 out of 40 couples) achieved pregnancy after a single embryo transfer in the first IVF cycle. However, in the main group, where homocysteine levels were corrected before treatment, the pregnancy rate increased to 60.0% (30 out of 50 couples, $p<0.05$). These findings confirm that homocysteine screening and targeted treatment before IVF can improve pregnancy success rates by up to 14%.

## Conclusion.

Overall, these results suggest that homocysteine regulation should be considered an essential component of pre-IVF assessment and treatment protocols, as it has the potential to enhance ART success rates and improve reproductive outcomes.

## References


1. Максудова М.М. Особенности стимуляции яичников у женщин старшего репродуктивного возраста в протоколах ЭКО/ИКСИ. – 2024
2. Agrawal A., Ilango K., Singh P.K. et al. Age dependent levels of plasma homocysteine and cognitive performance // Behav. Brain. Res. – 2015. – Vol. 283. – P. 139-144. doi: 10.1016/j.bbr.2015.01.016 https://onlinelibrary.wiley.com/doi/abs/10.1111/eci.13486
3. Berker B., Kaya C., Aytac R., Satiroglu H. Homocysteine concentrations in follicular fluid are associated with poor oocyte and embryo qualities in polycystic ovary syndrome patients undergoing assisted reproduction // Hum. Reprod. (Oxf.). – 2009. – Vol. 24. – P. 2293-2302. doi: 10.1093/humrep/dep069 https://pubmed.ncbi.nlm.nih.gov/19443458/

4. Chen L., Chen H., Wang X. et al. Association of homocysteine with IVF/ICSI outcomes stratified by MTHFR C677T polymorphisms: a prospective cohort study // Exp. Reprod. Biol. – 2021. – Vol. 43, №1. – P. 52-61. https://pubmed.ncbi.nlm.nih.gov/34016520/
5. Grandone E., Colaizzo D., Vergura P. et al. Age and homocysteine plasma levels are risk factors for thrombotic complications after ovarian stimulation // Hum. Reprod. – 2004. – Vol. 19. – P. 1796-1799. doi: 10.1093/humrep/deh346 https://pubmed.ncbi.nlm.nih.gov/15178664/ .
6. Manzur N.F., Gluska H., Feferkorn I. et al. // Gynecol. Endocrinol. Reprod. Med. – 2023. – Vol. 307. – P. 1975-1982. https://pmc.ncbi.nlm.nih.gov/articles/PMC11084717/
7. Razi Y., Eftekhar M., Fesahat F. et al. Concentrations of homocysteine in follicular fluid and embryo quality and oocyte maturity in infertile women: a prospective cohort // J. Obstet. Gynaecol. – 2021. – Vol. 41. – P. 588-593. doi: 10.1080/01443615.2020.1785409 https://pubmed.ncbi.nlm.nih.gov/32749170/
8. Wang F., Sui X., Xu N. et al. The relationship between plasma homocysteine levels and MTHFR gene variation, age, and sex in Northeast China // Niger J. Clin. Pract. – 2019. – Vol. 22. – P. 380-385. https://pubmed.ncbi.nlm.nih.gov/30837427
9. Yuldasheva S.Z. Kriokonservatsiya usullari va ularning odam embrioniing yashab qolishga ta'siri. – 2024