

ANNOTATION

of PhD thesis by **Suleimenova Meruyert**
**on the topic «Improving organizational principles in overcoming infertility
using assisted reproductive technologies»,**
submitted for the degree of Doctor of Philosophy (PhD) in the educational
programme 8D139 – «Public Health»

Relevance of the problem

According to a new report by the World Health Organisation (WHO), one in six couples suffer from lifetime infertility, corresponding to 17.5% of the adult population (WHO 2023). The frequency of infertile marriage in the Republic of Kazakhstan ranges from 12% to 15.5%. (V. Lokshin, I. Khoroshilova 2018). According to MICS (Multiple Indicator Cluster Survey) infertility was determined by the words of sexually experienced women aged 15-44 who reported trying unsuccessfully to get pregnant for two years or more: 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% (Ministry of National Economy of the Republic of Kazakhstan, Committee on Statistics 2019).

The incidence of female infertility in the republic was 56% of the total number of gynaecological diseases. According to the literature, infertility may be accompanied by the development of psycho-emotional problems, disturbance of sexual relations, difficulties in social adaptation and deterioration of the quality of life (Paskar S.S., Kalugina A.S., Tkachuk A.G. 2019) Meanwhile, the use of ART with positive outcomes significantly contributes to improving the quality of life of couples (W. Zdanowski et al. 2022),(G. Aimagambetova et al. 2020).

Over the last four decades, infertility treatments have been revolutionised significantly, mainly by assisted reproductive technologies (ART) such as in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI), cryopreservation of germ cells and embryos, surrogacy, preimplantation genetic testing (PGT). According to ICMART (International Committee for Monitoring Assisted Reproductive Technologies) with the help of ART (G.M. Chambers et al. 2021) more than 8 million babies have been born globally, the first being Louise Brown, born in 1978. Europe leads the world in the number of ART programmes performed, initiating about 50% of all reported cycles. The number of cycles performed in many developed countries has increased by 5-10% per year in the last few years (G. V Wyns C, De Geyter C, Calhaz-Jorge C, Kupka MS, Motrenko T, Smeenck J, Bergh C, Tandler-Schneider A, Rugescu IA, The European IVF-monitoring Consortium for the European Society of Human Reproduction and Embriology 2022).

ART has been developing rapidly in Kazakhstan since the first successful IVF case in 1996. The medical and social significance of infertility has increased, and its prevalence has worsened against the background of changes in reproductive behavior and a decrease in the birth rate (Ministry of National Economy of the Republic of Kazakhstan, Committee on Statistics 2019),(K. Urupina et al. 2022). Women who seek education, career and high social status are forced to change their

stance on the important issue of childbearing. Delaying childbearing until a later age substantially limits women's ability to carry out their reproductive function. This problem has widespread social consequences, as more and more women of late reproductive age seek treatment for infertility, and this alarming trend continues to increase (I.A. Zhabchenko, O.R. Syudmak 2019), (Solovyova T.V., Karaseva A.S. 2018), (G. Asadova 2021).

The infertility treatment availability indicator is a critical indicator that can help to identify barriers to care and guide health care development in this area (A. Affferri et al. 2022). Problems with availability, accessibility and quality of infertility interventions remain a problem in most countries. ART is still largely inaccessible in low- and middle-income countries (World Health Organization 2023). In a study of the affordability of ART, a number of authors have noted that medical fertility services are financially inaccessible to a large proportion of the population (E.M. Prokopov A.Y., Osmanov, R.R. Manyakov 2020), (Sh.K.K. V.N.Lokshin, M.D.Omar 2020). President of the Republic of Kazakhstan Kassym-Zhomart Tokayev in his Address to the people of Kazakhstan instructed to launch a special programme "Ansagan sabi" from 2021. The number of subsidizing programmes for IVF has increased to seven thousand. In 2020 the number of subsidizing programmes was 1,000 (The official website of the President of the Republic of Kazakhstan 2020).

Over the past decade, as the need for infertility treatment has increased, the use of ART in Kazakhstan has tended to grow, which requires the introduction of a national register of ART to monitor the quality of care provided. It is necessary to introduce indicators of the effectiveness of ART in order to improve the quality of services provided (T.M. Chiware et al. 2021), (S. Dyer et al. 2020).

Thus, a patient-centred approach to infertile couples, improving the continuity between primary health care (PHC) doctors and narrow specialists, increasing access to effective and safe infertility treatment by improving the organisation of ART treatment is an urgent problem, which determined the choice of the aim and objectives of this study.

Purpose of the thesis research:

To scientifically substantiate and develop a model for improving the organization of infertility treatment with assisted reproductive technology in the Republic of Kazakhstan.

The main objectives:

1. To conduct a dynamic analysis of the number, structure, outcomes of all ART cycles for the period 2010-2019 and an analysis of quota programs for the period 2018-2020 in the Republic of Kazakhstan.
2. To study the medical and social characteristics and assess the psycho-emotional status of women with infertility who are being treated with assisted reproductive technologies according to the FertiQoL questionnaire.
3. Evaluate the availability of infertility treatment through ART and develop indicators to assess the effectiveness of ART clinics.
4. To develop a model for improving the organization of treatment of infertility patients using assisted reproductive technologies and evaluate its effectiveness.

Methods of the study

The study was conducted according to the following methodology:

Study design - observational / analytical / cross-sectional study.

Reports of ART clinics from 2011 to 2019, and RCEZ reports.

Patients who have completed the IVF/ICSI program at the ICCR "Persona" clinic from all regions of Kazakhstan.

Subject of the study:

The results of socio-demographic data of patients, the psychoemotional status of women according to the FertiQoL questionnaire who passed the IVF/ICSI program, assessment of barriers to access to infertility treatment for patients who received funding under the CSHI.

Provisions for defense

1. The number of IVF/ICSI cycles is increasing annually in Kazakhstan, which requires monitoring of ART programmes to assess the performance of IVF clinics.
2. Women with infertility from rural areas have low psycho-emotional status prior to the ART programme compared to urban dwellers.
3. The results of the barrier analysis indicate a low availability of assisted reproductive technology infertility treatment.
4. The proposed model for improving the management of patients with assisted reproductive technology helps to improve the accessibility and quality of services.

Scientific novelty of the study

For the first time, a register for the ten-year period (2010-2019) has been published. A scientific analysis of the main indicators of the activity of ART clinics in the Republic of Kazakhstan was carried out.

The medical and social characteristics and quality of life of women requiring assisted reproductive technology infertility treatment were assessed using the FertiQoL questionnaire;

For the first time, the main barriers to the availability of assisted reproductive technology treatment for patients with infertility in the MRA setting have been identified.

For the first time in the Republic of Kazakhstan, the main indicators for assessing the performance of RTT clinics to improve the quality of services provided were identified based on the developed model.

For the first time, digital monitoring of ART cycles has been developed and implemented in the Republic of Kazakhstan;

A model for improving the organisation of infertility treatment with assisted reproductive technologies in the Republic of Kazakhstan has been developed and implemented on the basis of scientifically substantiated data.

Theoretical outcomes of the PhD work

The results of a 10-year analysis of the performance of ART clinics in Kazakhstan are important as a theoretical basis for developing strategies to improve the quality of reproductive health services.

The results of the FertiQoL methodology for assessing the quality of life of women facing infertility problems have theoretical relevance for further research on the psychological and social impact on patients during treatment, as well as for the development of prevention and support strategies.

Practical outcomes of the PhD work

- Developed and delivered online webinars once a quarter (ongoing training) for obstetricians and gynaecologists to improve diagnosis and treatment of infertility, further recommended for GPs;
- Guidelines on the management of infertility have been developed.
- An increase in the number of ART programmes and an expansion of the selection criteria for infertility provision under the MHI were recommended to the MHRC.
- Developed and implemented a digital register to monitor ART cycles; Recommended the introduction of compulsory register maintenance for the RC.
- Developed and implemented a questionnaire for patients in need of infertility treatment to determine psycho-emotional status and referral to a psychological support specialist (copyright №25647);
- Developed and recommended TRT performance evaluation indicators for self-evaluation and external evaluation of TRT clinics (copyright №34349)

The author's personal contribution includes the development of the theoretical and methodological programme of research, the organization and conduct of the study, direct participation in all stages of research, statistical processing of data, the writing of sections of the thesis, the interpretation and discussion of results, the formulation of defensive statements and conclusions and practical recommendations.

Conclusions

1. According to the results of our descriptive analysis of the number, structure, and outcomes of ART cycles for the period 2010 – 2019, the number of ART programs conducted has increased 6-fold. The frequency of selective single embryo transfer increased from 19.1% to 48.9%. The analysis of quota programs for the period from 2018 to 2020 showed high rates of cumulative pregnancy rate, on average reaching 45%. The frequency of multiple births was high and averaged 22.5%, which could contribute to the development of complications of pregnancy and childbirth.
2. The psychoemotional status of women with infertility referred for treatment with assisted reproductive technologies according to the FertiQoL questionnaire averaged 59.6 ± 11.5 . In rural respondents, the emotional scale (27.42 ± 9.59 vs. 63.86 ± 14.99 ; $p < 0.001$), the physical health scale (64.34 ± 18.41 vs. 38.21 ± 18.90 ; $p < 0.001$) and the social environment scale (64.75 ± 13.81 vs. 45.52 ± 14.34 ; $p < 0.001$) were statistically significantly lower than from urban residents.
3. Higher levels of access barriers were found among rural residents compared to urban residents in the block of awareness (29.7% of the rural population versus 25.6% of the urban population), accessibility (31.7% of the rural population versus 22.0% of the urban population), acceptability (17.5% of the rural

population versus 9.8% of the urban population), defined regions where there are no services for the treatment of infertility by ART methods.

4. The conceptual model of improving the organization of treatment of infertility patients using assisted reproductive technologies is a scientifically sound and effective tool for monitoring and implementing measures to increase the availability and improve the quality of specialized services. After the introduction of the model, the following changes were revealed: the number of cycles at the expense of the OSMS increased by 7 times and reached 7000 as a result of the implementation of the "Ansagan Sabi" program. After the introduction of psychological support in IVF programs, the patients' satisfaction level in the general FertiQoL scale increased by 8.2%. At the level of ART clinics, after the introduction of the digital register in 2020-2021, to monitor ART programs, the percentage of clinic participation increased from 50% in 2019 to 78% in 2022.

Published papers on the topic of the thesis

8 scientific papers have been published on the topic of the dissertation research, including:

1. In the Scopus database indexed journals – 2 publications
2. In the Committee for Quality Assurance in Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan recommended journals – 3 publications
3. In the international conference's collections – 2 theses
4. In the Republican journal - 1 publication

Approbation of the thesis

The study materials were presented and discussed at the following conferences:

XII Congress of the Kazakhstan Association of Reproductive Medicine, 15-16 November 2020 "Accessibility of Assisted Reproductive Technologies in Kazakhstan and worldwide" (Almaty);

XXXI Annual International Conference of the RAHR, 8-11 September 2021 "Assessment of quality of life of women with infertility by the Fertility quality of life questionnaire (FertiQoL)" (Sochi);

IVF worldwide online congress, 1 October 2021 "Evaluation of the quality of life of women according to the Fertility Quality of life tool" (UK);

XIII International Congress of the Kazakhstan Association of Reproductive Medicine, 15-16 November 2021 "Cumulative effectiveness of ART programmes by age group";

European Society of Human Reproduction and Embryology 38th Annual meeting, 3-6 July 2022 'Quality of life assessment of women undergoing in vitro fertilisation treatment in Kazakhstan' (Milan);

Innovative patents, copyright certificates

1. Author's certificate No. 25647 "Instrument for studying the quality of life of infertility patients in the Republic of Kazakhstan" 2022.
2. Author's certificate No. 34349 "Questionnaire on barriers to access of assisted reproductive technologies to infertile couples" 2023.

The results of this dissertation work have led to the development of

Methodological recommendations on examination and referral of women suffering from infertility for in vitro fertilization in the MHI system;

Methodological recommendations for assisted reproductive technology organizations on the introduction of performance evaluation indicators in order to improve the quality of services provided.

Records of the implementation of the results of the research work into the activities of health care practitioners

The scope and structure of the thesis.

The dissertation work is set out on 107 pages, the structure contains an introduction, 3 sections of the main chapters, a conclusion which sets out the main conclusions, practical recommendations and a list of references. There are 150 literary sources in the thesis, 24 of them are in Russian, 33 tables and 35 figures.