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Impact of governmental support to the IVF clinical pregnancy rates: differences between public and private clinical settings in Kazakhstan—a prospective cohort study

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ABSTRACT

Objectives Infertility rates have been increasing in low-income and middle-income countries, including Kazakhstan. The need for accessible and affordable assisted reproductive technologies has become essential for many subfertile women. We aimed to explore whether the public funding and clinical settings are independently associated with in vitro fertilisation (IVF) clinical pregnancy and to determine whether the relationship between IVF clinical pregnancy and clinical settings is modified by payment type.

Design A prospective cohort study.

Setting Three private and two public IVF clinics located in major cities.

Participants Women aged ≥18 seeking first or repeated IVF treatment and agreed to complete a survey were included in the study. Demographical and previous medical history data were collected from a survey, while clinical data from medical records. The total response rate was 14%.

Primary and secondary outcome measures Clinical pregnancy was defined as a live intrauterine pregnancy identified by ultrasound scan at 8 gestational weeks. The outcome data were missing for 22% of women.

Results Out of 446 women in the study, 68.2% attended private clinics. Two-thirds of women attending public clinics and 13% of women attending private clinics were publicly funded. Private clinics retrieved, on average, a higher number of oocytes (11.5±8.4 vs 8.1±7.2, p<0.001) and transferred more embryos (2.2±2.5 vs 1.4±1.1, p<0.001) and had a statistically significantly higher pregnancy rate compared with public clinics (79.0% vs 29.7%, p<0.001). Publicly funded women had on average a higher number of oocytes retrieved and a statistically significantly higher probability of clinical pregnancy (RR=1.23, 95% CI 1.02 to 1.47) than self-paid women, after adjusting for covariates. There was no statistically significant interaction between clinical setting and payment type.

Conclusions Private clinics and public funding were independently associated with higher IVF clinical pregnancy rates. There is also a need to further investigate whether the increase in public funding will influence clinical pregnancy rates.

Strengths and limitations of this study

- ► This is the first multicentre study investigating potential predictors for the in vitro fertilisation (IVF) outcomes between private and public clinical settings in Kazakhstan.
- ► Non-response bias may result in overestimation of the association between clinical settings and funding models with the IVF outcome because it is possible that non-respondents had a more likely poor prognosis.
- ► 22% of the study participants had unknown IVF outcomes and were excluded from the multivariable analysis.
- ► Although we controlled for several covariates in the models, inclusion of additional variables such as behavioural, environmental factors, parental demographical characteristics, embryo quality and other factors could benefit future research in obtaining less biased results.

INTRODUCTION

Infertility is defined as an inability to conceive within 12 months of an unprotected sexual intercourse in women younger than 35 years or within 6 months in women older than 35 years.[1 2] Infertility affects a significant proportion of the population around the globe, and it is estimated to affect between 8% and 12% of reproductive-aged couples worldwide.[3–5] However, in some developing countries, the rates of infertility are much higher, reaching 25%–30% in some populations.[3] It is estimated that more than 180 million couples in developing countries suffer from primary or secondary infertility.[6] Taking into consideration that the desire for parenthood is one of the basic human needs and rights, the worldwide infertility problem becomes even more dramatic. In most societies, despite cultural or religious preferences, becoming a parent is perceived as an essential component in achieving self-realisation and meaning in life.[7]

One of the most important issues in contemporary-assisted reproductive technologies (ART) markets is access to the treatment.[8 9] As infertility is a medical condition, and couples with unfavourable fertility characteristics should have equal access to receive medical care. Currently in many countries, healthcare policymakers are trying to increase access to ART treatment for patients who cannot afford to pay out of pocket for the treatment.[8] Moreover, the relative cost that patients pay for ART treatment predicts not only the level of access but also the number of embryos transferred.[9] This fact makes insurance or governmental support is very important. There is a huge demand and unmet need for ART, especially in developing countries with a high infertility rate.[6] A health economic report in 2002 put the lowest estimate of the global need for ART at 1500 cycles per million populations per year, assuming that only 50% of couples who need ART will have it done.[10] At the same time, there is a large difference in both infertility services availability and quality between high and low-income countries and between the rich and the poor within the same country,[11] particularly in ART procedures, which violates the basic ethical principles of justice, equity and equality.[8 11 12] However, some studies showed that insurance support to ART access can lead to a substantial increase in in vitro fertilisation (IVF) usage in a market;[8] therefore, controlling by specific patient selection is required. This will ensure that the treatment for couples with severe medical needs will be available.

Despite an increasing medical demand for infertility treatments, public funding challenges for IVF exist in many developing countries.[13] While high-income countries, like France, Spain and Israel, provide full coverage of IVF treatments as a part of social policy, low-income countries cannot afford it. In the situation when coverage for IVF is absent or incomplete, it makes the IVF treatments unaffordable for couples with the most need. From both the public health and economic standpoint, the financial support of IVF may represent a good investment in terms of governmental financial returns, even in lower income countries with state-financed healthcare systems such as Ukraine, Belarus and Kazakhstan.[13] There is an interest to support IVF treatments from a governmental perspective. After successful IVF treatment, subfertile couples give births to new citizens who will eventually become future taxpayers. However, access to IVF is dependent not only on the particular country income but also on the efficiency of wealth distribution, the health policy and health insurance system.[8 13]

Kazakhstan is a developing Central Asian republic, and one of the countries with the highest regional infertility prevalence.[3 13–16] Fertility as a cornerstone of family planning in Central Asian culture plays an important role in the strength of couples' relationships.[16] However, the fertility rate in Kazakhstan decreased significantly from 4.6 in 1960 to 2.8 in 2015,[15] and the infertility prevalence varies from 12% to 15.5%.[14–16] Considering the infertility issue in Kazakhstan, the need for accessible and affordable ART is found to be very high.

A pioneer clinic for IVF in Kazakhstan was established in 1995 with the first newborn delivered in 1996. The first ART clinic was private, and before 2010 all expenses for IVF treatment had been paid by patients. Since 2010, the Ministry of Healthcare provides funds for IVF coverage, and few public IVF clinics have been established. Apart from public IVF clinics, the public-funded IVF cycles are performed in private clinics as well. Although the funds are limited in amount, from 2010 through 2018 with the governmental support (quotas), around 3000 babies were born with IVF procedure facilitation. According to the Kazakhstan State Program, in 2021, the government has started funding 7000 IVF cycles per year.[17] It is seven times more than in 2020 (1000 cycles). Considering the mentioned circumstances, it is very important to investigate factors that might have an impact on the IVF outcome and to understand how effectively governmental money has been used.

We aimed in this study to investigate the following research questions: 'Are public funding and clinical settings independently associated with higher IVF clinical pregnancy rates?' and 'Is the relationship between IVF clinical pregnancy and clinical settings modified by payment type?'

METHODS

Study design

This prospective cohort study was conducted among women attending ART clinics between June 2019 and September 2020 in Kazakhstan. Women seeking first or repeated IVF treatment were asked to participate in the study, providing them with oral and written informed consent. The response rate was 14% (446 out of 3223). Adult women who were seeking IVF treatment and who were able to answer survey questions in Kazakh, Russian or English were included in the study. Women who were under 18 years old who were not able to answer the survey questions in Kazakh, Russian or English languages and who refused to provide written informed consent were excluded.

The study participants were enrolled from three private and two public ART clinics. All private clinics located in major cities are branches of one for-profit medical organisation. This private organisation was established in 1995 and performed the first IVF treatment in Kazakhstan. The public clinics were also from major cities—the National Research Center of Mother and Child Health in Nur-Sultan city and the Regional Perinatal Center in Aktobe city. The hospital-based public clinics have started providing ART treatment starting from 2007 and 2018, respectively. The National Research Center of Mother and Child Health was accredited and certified according to the Joint Commission International standards. Both private and public clinics are entitled to provide services paid out-of-pocket and under public funding.

IVF treatment is funded through public funding or self-payment (out-of-pocket). Subfertile patients could receive public funding for one IVF cycle per year within the State Guaranteed Health Benefits package of the Republic of Kazakhstan. To receive public funding, women must satisfy several inclusion criteria such as being Kazakhstani residents, being in the age range of 18–42 years old, having a good ovarian reserve, no severe comorbidities that could substantially reduce the probability of conceiving a child via IVF and no children. Women with ovarian or cervical benign or malignant tumours, acute inflammatory diseases, somatic or psychological diseases and low ovarian reserve do not fall under the government support. Only 15 clinics, 5 public and 10 private, are accredited to provide IVF services under the public funding scheme. On the other hand, self-paid women are not restricted in age, number of IVF cycles per year or clinical setting where to undergo IVF treatment. For self-paid women, costs associated with IVF treatment range between US$1200 and US$3600 per one IVF cycle.

Study variables

The binary outcome variable was clinical pregnancy that was defined as a live intrauterine pregnancy identified by ultrasound scan at 8 gestational weeks. The clinical pregnancy rate was calculated per egg retrieval cycle (cumulatively from fertilised fresh and frozen eggs). Patients were followed up for 3 months after an embryo(s) transfer. Patients with 'unknown' status were those who have not yet reached 8 weeks gestation and have not yet had an ultrasound to determine the presence or absence of clinical pregnancy. Patients provided sociodemographic data such as age in years, body mass index (BMI), education level and payment type (publicly funded or self-paid) through a survey. BMI was categorised as underweight (less than 18.5 kg/m^2), normal (18.5–24.9 kg/m^2) and overweight/obese (25 kg/m^2 and above). According to the International Standard Classification of Education (ISCED), education level was grouped to ISCED 4 level—secondary high school, ISCED 5 level—postsecondary non-tertiary education and ISCED 6 level—bachelor or master-level education. Patient's previous medical history data such as comorbidities associated with infertility, duration of infertility, number of previous deliveries, number of previous miscarriages, number of intentional pregnancy interruptions and number of previous IVF cycles were collected using a standardised survey. Clinical data about the number of oocytes retrieved, number of embryos transferred, cause of infertility (women, men and mixed), type of treatment protocol and multiple pregnancies were collected from patients' medical records.

Statistical analysis

In the descriptive analysis, continuous variables were summarised as means or medians and corresponding variability measurements (SD and IQs). Categorical variables were described in absolute and relative frequencies. To compare means between two groups, independent t test or Mann-Whitney U-test was used, where appropriate. To test independence between two categorical variables, the χ^2 test or Fisher's exact test was performed. Simple and multiple Poisson regression modelling with robust estimation were implemented to assess relationships of independent variables with the outcome variable. Since the number of oocytes retrieved is considered a strong predictor for the clinical pregnancy,[18 19] we additionally constructed linear regression models to test associations of independent variables with the number of oocytes retrieved. Models were built according to the parsimonious principle, including a reasonable number of covariates based on their clinical, epidemiological importance and statistical significance. We hypothesised that the payment type and clinical setting would be highly associated, and inclusion both would result in multicollinearity. However, no multicollinearity was observed. To check multicollinearity, we used the variance inflation factor and examined changes in coefficients and its SEs by adding and removing these variables from the models. We decided to include both variables in the regression modelling as private clinics look for additional income by treating publicly funded patients, likewise, public clinics are encouraged to provide out-of-pocket services. No interaction was observed between payment type and clinical setting at significance level of 0.05. Nonetheless, we presented results from the model with the interaction between clinical settings and payment type, as it was practically important to see whether the outcomes differ between private and public clinics depending on payment type. We also checked for other interactions. An interaction between comorbidity and the clinical settings was found statistically significant. Finally, we examined the goodness-of-fit of the final models using Pearson's and deviance goodness-of-fit tests. The goodness-of-fit statistics were non-significant, indicating that the models fitted well enough to the sample data.

Patient and public involvement

Patients and the public were not involved in the design and conduct of this research.

RESULTS

Four hundred and forty-six women attending IVF clinics agreed to participate in the study. The average age of the participants was 33.8±5.6 years (table 1). One-third of women were overweight or obese (27.9%), approximately half of them had education level at ISCED 6 (45.1%), and two-thirds paid themselves (out-of-pocket) for IVF treatment (67.9%). On average, infertility duration was 5.9±3.9 years (table 2). A female factor as a cause

Table 1 Sociodemographic characteristics of the study participants attending ART clinics between June 2019 and September 2020 in Kazakhstan.

Variable	All, N=446 (100%)	Public clinics, n=142 (31.8%)	Private clinics, n=304 (68.2%)	P value
Age (years), mean±SD	33.8±5.6	33.9±4.9	33.7±5.9	0.81
Missing data=2%				
BMI, n (%)				
Underweight	44 (11.0)	10 (7.3%)	34 (12.9%)	<0.01
Normal	245 (61.1)	76 (55.5%)	169 (64.0%)	
Overweight/obese	112 (27.9)	51 (37.2%)	61 (23.1%)	
Missing data=10%				
Education level, n (%)				
ISCED 4	120 (27.0%)	51 (36.4%)	69 (22.7%)	<0.01
ISCED 5	124 (27.9%)	26 (18.6%)	98 (32.2%)	
ISCED 6	200 (45.1%)	63 (45.0%)	137 (45.1%)	
Missing data=0.5%				
Location, n (%)				
Aktobe	67 (15.0%)	67 (47.2%)	0 (0%)	
Almaty	99 (22.2%)	0 (0%)	99 (32.6%)	
Nur-Sultan	183 (41.0%)	75 (52.8%)	108 (35.5%)	
Shymkent	97 (21.8%)	0 (0%)	97 (31.9%)	
Missing data=0%				
Payment type, n (%)				
Publicly funded	112 (32.1%)	85 (59.9%)	27 (13.0%)	<0.001
Self-paid	237 (67.9%)	57 (40.1%)	180 (87.0%)	
Missing data=21.8%				

BMI, body mass index; ISCED, International Standard Classification of Education.

of infertility was determined in half of the women, while in others, factor was mixed or men, and a quarter of the women had previously attempted at least one IVF cycle treatment (24.2%). Most women were treated with short or long classic protocol, and the cumulative pregnancy rate reached 62.2% (table 3).

Public versus private clinics

More than two-thirds of women attended private clinics (68.2%). There were no differences in age (p=0.81), infertility duration (p=0.75), number of previous miscarriages (p=0.21), number of previous intentional pregnancy interruptions (0.14) and number of previous IVF cycles (p=0.41) between participants of public and private clinics (table 2). Public clinics had statistically significantly higher proportions of overweight or obese women (p<0.01), patients with education level at ISCED 4 (p<0.01) and patients who were publicly funded (p<0.001) than private clinics. The proportion of patients with comorbidities was also higher in public clinics (58.4% vs 29.9%, p<0.001) than in private clinics. However, the percentage of women with a history of previous deliveries (p<0.001) and the proportion of patients who had a female factor as a cause of infertility (p<0.01) were statistically significantly higher among patients in private clinics. Private clinics retrieved, on average, a higher number of oocytes (11.5±8.4 vs 8.1±7.2, p<0.001), transferred more embryos (2.2±2.5 vs 1.4±1.1, p<0.001) and had more multiple pregnancies (0 vs 4, p=0.32) than public clinics (table 3). Private clinics had a statistically significantly higher cumulative pregnancy rate (79.0% vs 29.7%, p<0.001) and higher clinical pregnancy rate per embryos transferred (44.7% vs 22.0%, p<0.01) compared with public clinics.

Publicly funded versus self-paid

One-third of women (32.1%) received public funding for IVF treatment. There was no difference between publicly funded and self-paid patients in terms of age, BMI, comorbidity, number of previous miscarriages and number of previous intentional pregnancy interruptions (online supplemental tables 1,2). Despite that the number of oocytes retrieved, the number of embryos transferred and type of treatment protocol used were comparable in the two groups, cumulative clinical pregnancy rates were statistically significantly different between them (53.1% vs 65.2%, p=0.04, publicly funded vs self-paid, respectively, online supplemental table 3).

Table 2 Past IVF medical history of the study participants attending ART clinics between June 2019 and September 2020 in Kazakhstan.

Variable	All, N=446 (100%)	Public clinics, n=142 (31.8%)	Private clinics, n=304 (68.2%)	P value
Comorbidity, n (%)				
Yes	174 (39.0%)	83 (58.4%)	91 (29.9%)	<0.001
No	272 (61.0%)	59 (41.6%)	213 (70.1%)	
Missing data=0%				
Infertility duration (years)				
Mean±SD	5.9±3.9	6.0±3.5	5.9±4.1	0.75
Median (IQR)	5 (3–8)	6 (3–8)	5 (3–8)	
Missing data=5.6%				
Number of previous deliveries, n (%)				
None	298 (67.1%)	106 (74.6%)	192 (63.6%)	<0.001
One	112 (25.2%)	36 (25.4%)	76 (25.2%)	
Two or more	34 (7.7%)	0 (0%)	34 (11.2%)	
Missing data=0.5%				
Number of previous miscarriages, n (%)				
None	384 (86.5%)	127 (89.4%)	257 (85.1%)	0.21
One or more	60 (13.5%)	15 (10.6%)	45 (14.9%)	
Missing data=0.5%				
Number of previous intentional pregnancy interruptions, n (%)				
None	404 (91.0%)	125 (88.0%)	279 (92.4%)	0.14
One or more	40 (9.0%)	17 (12.0%)	23 (7.6%)	
Missing data=0.5%				
Number of previous IVF cycles, n (%)				
None	335 (75.8%)	106 (75.2%)	229 (76.1%)	0.41
One	67 (15.2%)	25 (17.7%)	42 (13.9%)	
2 or more	40 (9.0%)	10 (7.1%)	30 (10.0%)	
Missing data=0.9%				
Cause of infertility, n (%)				
Female	218 (49.3%)	57 (40.4%)	161 (53.5%)	<0.01
Male	41 (9.3%)	8 (5.7%)	33 (11.0%)	
Mixed	183 (41.4%)	76 (53.9%)	107 (35.5%)	
Missing data=0.9%				

IVF, in vitro fertilisation.

Factors associated with IVF outcomes

In bivariable analysis, clinical pregnancy was statistically significantly associated with BMI, education level, location, type of payment, history of comorbidity, number of previous IVF cycles and number of oocytes retrieved during IVF treatment (online supplemental tables 4–6).

Public clinics on average retrieved a lower number of oocytes than private clinics (estimated β coefficient=−5.6, 95% CI −7.8 to −3.4) controlling for payment type and other covariates (table 4). While adjusting for the number of oocytes retrieved, the number of embryos transferred and payment type, IVF procedures in public clinics were independently negatively associated with the clinical pregnancy (RR=0.39, 95% CI 0.29 to 0.52). Women who were publicly funded for IVF treatment had on average a higher number of oocytes retrieved (estimated β coefficient=3.3, 95% CI 1.1 to 5.5) and a statistically significantly higher probability of clinical pregnancy (RR=1.23, 95% CI 1.02 to 1.47) than those who were self-paid in the multiple regression models.

Even though the relationship between clinical settings and the IVF clinical pregnancy rate was not modified by the payment type (p=0.19), we noticed that women who paid out of pocket had a stronger negative association with the IVF clinical pregnancy rate (and had a relatively lower number of oocytes retrieved) than patients who were publicly funded, among women who attended public clinics (table 5). There was, additionally, a statistically

Table 3 Clinical IVF characteristics of the study participants attending ART clinics between June 2019 and September 2020 in Kazakhstan.

Variable	All, N=446 (100%)	Public clinics, n=142 (31.8%)	Private clinics, n=304 (68.2%)	P value
Number of oocytes retrieved				
Mean±SD	10.5±2.0	8.1±7.2	11.5±8.4	<0.001
Median (IQR)	1 (0–2)			
Missing data=9%				
Number of embryos transferred				
Mean±SD	2.0±2.2	1.4±1.1	2.2±2.5	<0.001
Median (IQR)	2 (1–2)	1 (1–2)	2 (1–2)	
Missing data=14.8%				
Used protocol				
Classic-long	36 (8.3%)	5 (3.7%)	31 (10.3%)	0.06
Classic-short	379 (86.9%)	122 (90.4%)	257 (85.4%)	
Non-classic—natural cycle	7 (1.6%)	2 (1.5%)	5 (1.7%)	
Non-classic—ultrashort	13 (3.0%)	5 (3.75)	8 (2.7%)	
Non-classic—stimulated in luteal phase	1 (0.2%)	1 (0.7%)	0 (0%)	
Missing data=2.2%				
Clinical pregnancy, n (%)				
Yes	216 (62.2%)	35 (29.7%)	181 (79.0%)	<0.001
No	131 (37.8%)	83 (70.3%)	48 (21.0%)	
Missing data=22.2%				
Clinical pregnancy rate per embryos transferred, %	38.3	22.0	44.7	<0.01
Missing data=22.2%				
Multiple pregnancies, n (%)				
Yes	4 (1.0%)	0 (0%)	4 (1.4%)	0.32
No	418 (99.0%)	131 (100%)	287 (98.6%)	
Missing data=5%				

IVF, in vitro fertilisation.

significant interaction between clinical settings and comorbidity in predicting IVF clinical pregnancy. The adjusted relative risk of clinical pregnancy between public clinics versus private clinics among patients with no history of comorbidities was 0.72 (0.54 to 0.95), while among those with a history of at least one comorbidity was 0.13 (0.07 to 0.26) adjusted for covariates.

DISCUSSION

This is the first multicentre study conducted comparing IVF outcomes between private and public clinics in Kazakhstan. The study results show that the private clinics had a significantly higher clinical pregnancy rate. This difference could be partially explained by the more rigorous selection of subfertile women with better IVF prognosis in private clinics. Indeed, our study results confirm it: the private clinics had a lower percentage of overweight or obese women and a lower proportion of women with comorbidities than public clinics. Previous studies have shown that higher BMI levels and infertility-related comorbidities were negatively predictive of IVF outcomes.[18 20] In addition, the private clinics retrieved and transferred a statistically significantly higher number of oocytes and embryos, respectively. A systematic review and meta-analysis by Van Loendersloot *et al* illustrated that a higher number of oocytes retrieved, and a higher number of embryos transferred were positively associated with successful IVF outcomes.[18] As treatment costs per IVF cycle are high, patients in private clinics want to maximise the likelihood to conceive a child by retrieving and transferring more oocytes and embryos in a given IVF cycle.[21] However, transferring more embryos is associated with multiple gestation pregnancies.[22] Indeed, our study results found that all multiple gestation pregnancies occurred among women attending private clinics. Multiple gestation pregnancies are not only associated with higher risks of morbidity and mortality for mothers during pregnancy[23] but also with greater total pregnancy

Table 4 Simple and multiple linear and Poisson regression analyses of clinical settings and payment type predicting the number of oocytes retrieved and IVF clinical pregnancy using data collected among women attending ART clinics between June 2019 and September 2020 in Kazakhstan.

	Number of oocytes retrieved		Clinical pregnancy	
	Crude β-coefficient (95% CI)	Adjusted β coefficient (95% CI)*	Crude RR (95% CI)	Adjusted RR (95% CI)†
	Model 1		Model 3	
Private clinics	Reference	Reference	Reference	Reference
Public clinics	–3.4 (–5.1 to –1.7)	–3.7 (–5.5 to 1.9)	0.38 (0.26 to 0.54)‡	0.44 (0.33 to 0.59)‡
	Model 2		Model 4	
Private clinics	Reference	Reference	Reference	Reference
Public clinics	–3.4 (–5.1 to –1.7)	–5.6 (–7.8 to –3.4)‡	0.38 (0.26 to 0.54)‡	0.39 (0.29 to 0.52)‡
Self-paid	Reference	Reference	Reference	Reference
Publicly funded	–0.2 (–2.0 to 1.7)	3.3 (1.1 to 5.5)‡	0.82 (0.59 to 1.12)	1.23 (1.02 to 1.47)‡

*Each of the models was adjusted for age, BMI, education, comorbidity, cause of infertility, infertility duration, and number of previous IVF cycles.
†The model was adjusted for age, BMI, education, comorbidity, cause of infertility, infertility duration, number of previous IVF cycles, number of embryos transferred and number of oocytes retrieved.
‡P<0.05.
IVF, in vitro fertilisation; RR, relative risk.

costs, antenatal care and delivery costs when compared with singleton births.[24] Introduction of insurance coverage or public funding of reproductive treatment in many countries has resulted in the reduction of the number of embryos transferred per cycle, consequently, decreased incidence rates of multiple pregnancies[21 25 26] and reduced associated healthcare and patient costs.

After controlling for covariates, patients in public clinics still were less likely to conceive a child than patients in private clinics. Independent from the number of oocytes retrieved and number of embryos transferred, public clinics had lower clinical pregnancy rates. To obtain more robust results, further sensitivity analysis was performed (online supplemental table 7). To minimise selection bias in the results, 108 patients from one private clinic with the extremely high pregnancy rate (98.1%) were excluded from the further analysis.[16] The sensitivity analysis revealed that the public clinics were still independently associated with lower clinical pregnancy rates across all multiple regression models, which were adjusted for the same covariates.

Given that we controlled for important confounding variables in the models, lower pregnancy rates in public clinics could be potentially attributed to other factors. For example, patient's socioeconomic status could be one of them. Patients with lower socioeconomic status are likely to attend public IVF clinics and have poor reproductive prognosis than patients with higher socioeconomic status.[27] Previous studies have shown that patients from poor socioeconomic communities had lower levels of anti-Mullerian hormone and antral follicle count, indicating reduced ovarian reserve and a lower probability of conceiving a child.[28] Also, several studies have suggested that a 'physician factor' is an important predictor of

Table 5 The relationship of clinical settings modified by the funding model with the number of oocytes retrieved and IVF clinical pregnancy using multiple linear and Poisson regression analyses using data collected among women attending ART clinics between June 2019 and September 2020 in Kazakhstan.

	Adjusted β coefficient (95% CI) for number of oocytes retrieved*			Adjusted RR (95% CI) for clinical pregnancy†		
	Publicly funded	Self-paid	P value	Publicly funded	Self-paid	P value
Private clinics	Reference	Reference	0.10	Reference	Reference	0.19
Public clinics	–3.31 (-6.81 to 0.19)	–6.86 (-9.49 to –4.22)		0.46 (0.33 to 0.64)	0.30 (0.17 to 0.54)	

P values are calculated for interaction terms.
*Each of the models was adjusted for age, BMI, education, comorbidity, cause of infertility, infertility duration, and number of previous IVF cycles.
†The model was adjusted for age, BMI, education, comorbidity, cause of infertility, infertility duration, number of previous IVF cycles, number of embryos transferred and number of oocytes retrieved.
‡P<0.05.
BMI, body mass index; IVF, in vitro fertilisation; RR, relative risk.

successful IVF outcomes[29] align with the number of oocytes retrieved,[30] number of high-quality embryos transferred and absence of blood or mucus on the transfer catheter.[31] Finally, private clinics potentially continuously update their equipment to provide advanced and high technology care. Latest technologies foster patient-centred care by allowing more data collection that can be used for personalised and more effective IVF treatment.

Based on previous studies, we expected that publicly funded women would have a lower pregnancy rate than women who self-paid because public funding eliminates barriers related to treatment costs and encourages women with worse prognoses to seek IVF treatment.[21 25 26] However, public funding is not widely available in Kazakhstan and only a small percentage of subfertile women receive funding. Thus, those who are selected to receive state funding usually have a higher probability of conceiving a child.[32] Indeed, our study results showed that publicly funded women had a higher likelihood of conceiving a child than self-paid women. Bureaucratic barriers, in addition, discourage financially disadvantaged patients from applying for public funding and seeking IVF treatment. While financially independent patients who do not meet public funding criteria—because of their worse reproductive prognosis—seek IVF treatment by paying out-of-pocket. This speculation is supported by the findings from the multiple linear regression modelling factors associated with the number of oocytes retrieved. In the linear model, independent from other factors, patients who were publicly funded had a higher number of oocytes retrieved than self-paid women which indicates that self-paid patients had reduced ovarian reserve, thus, the lower probability to become pregnant.[19] It is likely that when public funding becomes more widely available in Kazakhstan, the utilisation of IVF services will increase and not only women with better reproductive prognoses will access IVF treatment but also patients with poor prognosis. Thus, the relative number of women with poor reproductive prognoses is expected to proportionally increase.[33] Self-paid patients and the government could consider other alternative fertility options. Intrauterine insemination could be an alternative fertility treatment as it has shown to be more cost-effective and associated with lower risks, and, most importantly, its success rate is quite comparable to IVF treatment.[34]

Since government-funded IVF cycles can be performed in both clinical settings as the government encourages the private sector to provide healthcare services under the governmental support and similarly, the public sector is stimulated to provide services on a self-paid basis, it was of the study interest to investigate the interaction between clinical settings and funding type in predicting the IVF outcome. Despite that the interaction between clinical setting and payment type was not statistically significant, we found that among self-paid women attending public clinics had a stronger negative association with IVF outcomes (relatively lower number of oocytes retrieved and lower clinical pregnancy rates) than among women who were publicly funded. There is a need to conduct further studies to investigate the existence of the interaction between the clinical settings and payment type among IVF patients. Also, we found that patients with a history of at least one comorbidity and attending public clinics had the lowest probability of conceiving a child. Patients with more severe comorbidities likely undergo IVF cycles in public clinics because they might have been refused to be treated in private clinics—the more rigorous selection process of subfertile women with better IVF prognosis is in place. Previous studies have shown that medical comorbidities were negatively associated with IVF pregnancy rates.[35 36] However, none of the studies examined the effect modification of medical comorbidities on the relationship between clinical setting and IVF outcomes.

Strengths and limitations

This is the first multicentre study investigating IVF clinical pregnancy rates between private and public clinical settings and between self-paid and publicly funded subfertile patients in Kazakhstan. The multivariable analysis that included clinically and epidemiologically important variables in the models allowed us to examine independent relationships of the clinical settings and payment type with the IVF outcomes.

Several study limitations that should be mentioned. First, non-response bias could be presented as the response rate was very low (14%). Since descriptive data on non-respondents were not collected for comparison, we were not able to confirm or exclude non-response bias. Overall, given the low response rate, the generalisability of the study results should be considered with caution. Second, 22% of the study participants had missing IVF outcome data. The associations of the IVF outcomes with clinical settings could be overestimated, as women with unknown IVF outcomes, who were not included in the multivariable analysis, had poor prognosis (were likely overweight or obese, had the longest infertility duration and a higher proportion of those who previously attempted IVF cycles).[37] Third, other important variables that could potentially confound the relationships were not collected. Although we controlled for several covariates in the models, inclusion of additional variables (behavioural factors such as smoking, alcohol consumption, physical activity; environmental factors; parental demographical characteristics; embryo quality; experience and qualification of physicians and number of times embryos transfers were performed within one egg retrieval cycle) could benefit future research in obtaining less biased results. Last, the small sample size in the regression models did not allow to obtain more robust estimates of the associations of clinical settings and payment type with IVF clinical pregnancy.

Conclusions

Private clinics and public funding were independently associated with higher IVF clinical pregnancy rates. Private clinics had a lower proportion of overweight or obese women and a lower proportion of women with comorbidities than public clinics. Private clinics retrieved, on average, higher number of oocytes and had higher multiple gestation pregnancy rate than public clinics. Women with better prognosis were likely selected to receive the IVF treatment through public funding. There is a need to further investigate what improvements are needed in the public funding sector to increase the clinical pregnancy rates among subfertile women.

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