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ASSISTED REPRODUCTION TECHNOLOGIES

Impact of maternal education level on live birth rate after in vitro fertilization in China: a retrospective cohort study

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Abstract

Purpose To assess the association between maternal education level and live birth after in vitro fertilization (IVF).

Methods We studied women who underwent the first cycle of fresh or frozen-thawed embryo transfer between 2014 and 2019. Women were divided into four educational categories according to the level of education received (elementary school graduate or less, middle school graduate, high school graduate, college graduate or higher). The live birth rate was compared between different education level groups. We used logistic regression to analyze the association between maternal education level and live birth after IVF.

Results We studied 41,546 women, who were grouped by maternal educational level: elementary school graduate or less ($n=1590$), middle school graduate ($n=10{,}996$), high school graduate ($n=8354$), and college graduate or higher ($n=20{,}606$). In multivariable logistic regression analysis, we did not demonstrate a statistically significant relationship between educational level and live birth in middle school graduate (adjusted odds ratio [AOR] 0.96; 95% confidence interval [CI], 0.84–1.09), high school graduate (AOR 1.01; 95% CI, 0.87–1.14) or college graduate or higher (AOR 1.01; 95% CI, 0.88–1.14) patients, with elementary school graduate or less as the reference group.

Conclusions Maternal educational level was not associated with the likelihood of live birth in patients undergoing fresh or frozen embryo transfer.

Keywords Educational status · In vitro fertilization · Pregnancy rate

Introduction

Educational level has been shown to be an independent factor in access to and outcomes of health care [1]. According to the World Health Organization (WHO), lack of education is one of the contributing factors to increased maternal and child mortality and morbidity in developing countries [2]. In general, better education has been shown to have a positive impact on different health issues [3].

Education influences lifestyles and social attitudes. Women with a higher education level are more likely to postpone marriage and childbearing [4]. Since female age is the main factor in infertility, higher educated women therefore comprise a large proportion of the in vitro fertilization (IVF) patient population. In addition, the expansion of higher educational attainment in women is a trend for the future [5]. Women with higher education levels are more likely to correctly perform IVF protocol, which may improve their clinical outcomes [6]. Several studies have suggested the association between healthier lifestyle behaviors and higher education attainment [7–9]. A better understanding of the association between education attainment and IVF outcomes would have broad social importance [10]. However, association between education and outcomes of IVF has rarely been studied. Assessing the impact of maternal education level on reproduction outcomes may provide opportunities to identify deficiencies in maternal knowledge and modify them through counseling [11].

The aim of this study was to determine the association between maternal education level and live birth after IVF.

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Materials and methods

Study design and patients

This retrospective cohort study includes women who underwent fresh or frozen-thawed embryo transfer between January 2014 and December 2019 in the Center for Assisted Reproductive Technology of Northwest Women's and Children's Hospital, China. All women were followed up for 1 year after embryo transfer. The study protocol was approved by the ethics committee of Northwest Women's and Children's Hospital (No. 2019013). Because of the retrospective character of the study, informed consent was waived. Patient data were anonymized. Women who underwent the first cycle of fresh or frozen-thawed embryo transfer (FET) were eligible to participate. We excluded women with no embryo transferred. The women were divided into four educational categories according to the level of education received (elementary school graduate or less, middle school graduate, high school graduate, college graduate or higher).

IVF protocol

Doctors chose different IVF protocols based on the patient's age and ovarian reserve. The gonadotropin-releasing hormone (GnRH) agonist and GnRH antagonist protocols have been the main protocol in our center. Controlled ovarian hyperstimulation, oocyte retrieval, embryo transfer, and endometrial preparation for frozen-thawed embryo transfer (FET) were performed as previously described [12, 13]. Briefly, for the GnRH agonist, patients used down-regulation from the mid-luteal phase of the previous cycle, recombinant FSH was started at 150–225 IU/day when the pituitary had reached desensitization. For the GnRH antagonist protocol, recombinant FSH was initiated on day 2 of the cycle. GnRH antagonist was started when the dominant follicle reached 12–14 mm at 250 mg/day. When two or more follicles reached 18 mm, human choronic gonadotropin (hCG) was administrated at a dose of 4000 to 10,000. Oocyte retrieval was carried out 34–36 h following hCG trigger. Conventional IVF or intracytoplasmic sperm injection (ICSI) was performed according to the male partner's semen quality. The criteria for ICSI use were abnormal semen parameters, preimplantation genetic testing (PGT) cycles, average fertilization rate < 30% with conventional insemination, high sperm DNA fragmentation, idiopathic infertility or long-term infertility. Women with ovarian hyperstimulation syndrome (OHSS), high progesterone level on hCG trigger day, untreated endocrinal disease, and PGT cycles had their embryos frozen and transferred in the subsequent cycle.

Outcome variables assessed

Live birth was defined as the delivery of at least one live-born baby at greater than 24 weeks of gestational age [14]. Clinical pregnancy was defined as a pregnancy diagnosed by ultrasonographic visualization of one or more gestational sacs or definitive clinical signs of pregnancy. Miscarriage was defined as a fetus or embryo removed or expelled from the uterus during the first half of gestation—20 weeks or less, or in the absence of accurate dating criteria, born weighing < 500 g. Preterm birth was defined as a birth that takes place after 24 weeks and before 37 completed weeks of gestational age.

Statistical analysis

Categorical variables were expressed as the number of cases (*n*) and percentage of occurrence (%). The numerical data are presented as the mean ± SD and differences in parameters between the groups were compared using independent sample *t*-tests or χ^2 tests as appropriate. Univariate and multivariable regression analyses were performed to determine the association between education level and live birth, excluding the interference of confounding factors. If adding a covariate to the model changed the estimated effect of a woman's educational level on live birth by 10% or more, the covariate was considered a confounder of the relationship between the woman's educational level and live birth and was included in the final multivariable models. We calculated crude odds ratios (ORs) and adjusted ORs (aORs) with a 95% confidence interval (CI). Interaction and stratified analyses were conducted according to confounders. Data were analyzed with the use of the statistical packages R (The R Foundation; http://www.r-project.org; version 3.4.3) and Empower (R) (www.empowerstates.com, X&Y solutions, inc. Boston, Massachusetts). The level of significance was set at $p < 0.05$.

Results

Table 1 shows the baseline characteristics. We identified 41,546 women who met the study criteria, of which 1590 women had completed elementary school graduate or less, 10,996 women had completed middle graduate education, 8354 women had completed high school graduate, and 20,606 women had completed college graduate or higher.

There were significant differences in baseline characteristics between groups, with elementary school or less education level women and men being older ($p < 0.001$),

Table 1 Baseline characteristics

Education level	Elementary school graduate or less ($n=1590$)	Middle school graduate ($n=10,996$)	High school graduate ($n=8354$)	College graduate or higher ($n=20,606$)	p value
Male age (years)	33.76 ± 3.29	31.98 ± 3.21	31.03 ± 3.92	32.94 ± 3.61	< 0.001
Semen volume (ml)	1.72 ± 0.57	1.81 ± 0.64	1.77 ± 0.34	1.79 ± 0.73	0.837
Semen concentration (10^6/ml)	55.17 ± 32.44	56.43 ± 33.63	56.14 ± 32.68	55.45 ± 33.51	0.638
Progressively motile sperm (%)	52.46	51.73	52.58	52.49	0.375
Female age (years)	32.71 ± 5.63	29.84 ± 4.80	29.83 ± 4.59	31.34 ± 3.96	< 0.001
Infertility duration (years)	5.92 ± 4.52	4.10 ± 2.97	3.62 ± 2.52	3.11 ± 2.09	< 0.001
BMI (kg/m^2)	23.53 ± 3.43	22.90 ± 3.47	22.57 ± 3.40	22.14 ± 3.12	< 0.001
Endometrial thickness (mm)	11.53 ± 3.44	11.31 ± 2.16	11.23 ± 2.67	11.25 ± 2.21	< 0.001
No. of oocyte retrieved	11.18 ± 6.38	12.08 ± 6.45	11.85 ± 6.28	11.57 ± 6.27	< 0.001
Infertility type					< 0.001
Primary infertility	665 (42.06%)	5456 (49.97%)	4380 (52.65%)	12,216 (59.65%)	
Secondary infertility	916 (57.94%)	5462 (50.03%)	3939 (47.35%)	8264 (40.35%)	
Protocol in the fresh cycle					< 0.001
Agonist	1245 (78.30%)	9052 (82.32%)	6832 (81.78%)	16,621 (80.66%)	
Antagonist	278 (17.48%)	1641 (14.92%)	1274 (15.25%)	3257 (15.81%)	
Other	67 (4.21%)	303 (2.76%)	248 (2.97%)	728 (3.53%)	
Fertilization type					< 0.001
IVF	1219 (76.71%)	8390 (76.38%)	6335 (75.92%)	15,591 (75.75%)	
ICSI	327 (20.58%)	2318 (21.10%)	1840 (22.05%)	4620 (22.45%)	
Half-ICSI	43 (2.71%)	276 (2.51%)	169 (2.03%)	372 (1.81%)	
Time of transfer					< 0.001
Fresh embryo transfer	781 (49.12%)	4996 (45.43%)	3963 (47.44%)	9868 (47.89%)	
FET	809 (50.88%)	6000 (54.57%)	4391 (52.56%)	10,738 (52.11%)	
No. of embryo transferred					0.206
1	656 (41.28%)	4731 (43.04%)	3632 (43.49%)	9012 (43.76%)	
2	926 (58.28%)	6227 (56.66%)	4687 (56.12%)	11,528 (55.97%)	
3	7 (0.44%)	33 (0.30%)	33 (0.40%)	55 (0.27%)	
Live birth	739 (46.48%)	5781 (52.57%)	4473 (53.54%)	10,923 (53.01%)	< 0.001
Birth weight (kg)	3.11 ± 0.59	3.13 ± 0.61	3.14 ± 0.62	3.82 ± 0.48	0.500
Miscarriage	112 (13.41%)	935 (16.93%)	683 (15.74%)	1701 (15.73%)	0.037
Preterm birth	144 (9.06%)	1063 (9.67%)	858 (10.27%)	2105 (10.22%)	0.204
Clinical pregnancy	883 (55.53%)	6959 (63.29%)	5339 (63.91%)	12,995 (63.07%)	< 0.001
Mode of delivery					< 0.001
Vaginal	159 (21.46%)	1379 (23.84%)	1108 (24.75%)	3046 (27.87%)	
Cesarean section	582 (78.54%)	4405 (76.16%)	3368 (75.25%)	7884 (72.13%)	
Fetal gender					0.342
Female	348 (46.96%)	2604 (45.01%)	2033 (45.41%)	5063 (46.33%)	
Male	393 (53.04%)	3181 (54.99%)	2444 (54.59%)	5866 (53.67%)	

BMI body mass index, *IVF* in vitro fertilization, *ICSI* intracytoplasmic sperm injection, *FET* frozen embryo transfer

Data are presented as % (n) or mean ± SD; significance for differences was measured using chi-squared test, Kruskal–Wallis

having longer infertility duration ($p < 0.001$), higher BMI ($p < 0.001$), more secondary infertility ($p < 0.001$), IVF insemination ($p < 0.001$), and fresh embryo transfer ($p < 0.001$). Elementary school or less education level women with less no. of oocyte retrieved ($p < 0.001$) and adopted more agonist protocol in the fresh cycle ($p < 0.001$). The live birth rates were lowest in elementary school or less education level women ($p < 0.001$). Miscarriage rates were also lowest in elementary school or less education level women ($p = 0.037$). Clinical pregnancy rates in elementary school graduate or less were lower compared to other groups ($p < 0.001$).

Table 2 shows the results of the univariable analysis. Female age, infertility duration, BMI, secondary infertility,

Table 2 Univariate analysis for live birth rate

Covariate	Statistics	OR (95%CI)	*p* value
Female age (years)	30.69 ± 4.47	0.92 (0.92, 0.92)	< 0.001
Infertility duration (years)	3.58 ± 2.64	0.96 (0.95, 0.97)	< 0.001
BMI (kg/m^2)	22.48 ± 3.31	0.98 (0.98, 0.99)	< 0.001
Endometrial thickness (mm)	11.27 ± 2.35	1.04 (1.03, 1.05)	< 0.001
No. of oocyte retrieved	11.75 ± 6.33	1.04 (1.04, 1.04)	< 0.001
Infertility type			
Primary infertility	22,717 (55.01%)	Reference	
Secondary infertility	18,581 (44.99%)	0.78 (0.75, 0.81)	< 0.001
Protocol in the fresh cycle			
Agonist	33,750 (81.24%)	Reference	
Antagonist	6450 (15.52%)	0.55 (0.52, 0.58)	< 0.001
Other	1346 (3.24%)	0.38 (0.34, 0.43)	< 0.001
Fertilization type			
IVF	31,535 (75.99%)	Reference	
ICSI	9105 (21.94%)	1.04 (0.99, 1.09)	0.106
Half-ICSI	860 (2.07%)	1.03 (0.90, 1.18)	0.682
Time of transfer			
Fresh embryo transfer	19,608 (47.20%)	Reference	
FET	21,938 (52.80%)	0.92 (0.89, 0.96)	< 0.001
No. of embryo transferred			
1	18,031 (43.42%)	Reference	
2	23,368 (56.27%)	1.31 (1.26, 1.36)	< 0.001
3	128 (0.31%)	0.71 (0.50, 1.01)	0.060

OR odds ratio, *CI* confidence interval, *BMI* body mass index, *IVF* in vitro fertilization, *ICSI* intracytoplasmic sperm injection, *FET* frozen embryo transfer

antagonist, and other protocol in the fresh cycle and frozen embryo transfer were negatively associated with live birth, while endometrial thickness, no. of oocyte retrieved, and double embryo transfer were positively associated with live birth. Interaction and stratified analyses were shown in Table S1. There were no significant interactions in any of the subgroups ($p > 0.05$ for all comparisons).

Compared with women with an education corresponding to elementary school graduate or less, there was an increased rate of live birth among women with higher educational levels in the crude model (Table 3). However, after adjusting for female age, infertility duration, BMI, endometrial thickness, no. of oocyte retrieved, infertility type, protocol in the fresh cycle, fertilization type, time of transfer, and no. of embryo transferred, women's educational level was not associated with live birth.

Discussion

In this retrospective cohort study of 41,546 women undergoing IVF with embryo transfer, we showed that different female educational levels were not associated with live birth.

Strengths of our study include its large sample size, incorporation of women of all age ranges, and representation of patients from the full spectrum of IVF protocols. Another advantage of this study was that it included only single-center cycles, which minimized potential bias (e.g., laboratory conditions and the protocol of IVF). In addition, we adjusted more variables to make the result more reliable.

There are some limitations to this study, such as its retrospective nature, which reduces its direct application to clinical practice. Interpretation of the results must take into account the fact that the study was restricted to patients who underwent IVF with at least a basic level of income and equal access to health facilities, since IVF treatment is not free and not covered by insurance in China. In addition, Internet literacy may be a bias since some less-educated women may get more information from the Internet.

Higher educational level has been found to be related to lower incidence and prevalence of cardiovascular diseases, diabetes, cancers, and chronic respiratory diseases [15]. Higher educational level is also associated with better use of healthcare services [16], more disease prevention in terms of

Table 3 Relationship between education level and live birth in different models

Education level	Crude model[a]		Adjusted model[b]	
	OR (95%CI)	*p* value	OR (95%CI)	*p* value
Elementary school graduate or less	Reference		Reference	
Middle school graduate	1.28 (1.15, 1.42)	< 0.001	0.96 (0.84, 1.09)	0.539
High school graduate	1.33 (1.19, 1.48)	< 0.001	1.01 (0.87, 1.14)	0.987
College graduate or higher	1.30 (1.17, 1.44)	< 0.001	1.01 (0.88, 1.14)	0.947

OR odds ratio, *CI* confidence interval

[a]We did not adjust other covariates

[b]Adjusted for female age, infertility duration, BMI, endometrial thickness, no. of oocyte retrieved, infertility type, protocol in the fresh cycle (agonist, antagonist, other), fertilization type, time of transfer and no. of embryo transferred

screening for sexually transmitted disease [17], and a lower risk of low 5-min Apgar score [18]. However, few studies have focused on the relationship between maternal educational level and live birth after IVF.

In general, women with higher education are more likely to be involved in healthy behavior such as regular exercise, a healthy diet, and regular check-up. Maternal educational level has been shown to be a strong predictor of seeking medical help with infertility [19]. However, the need and importance of ensuring fertility education is tailored to different women. At the same time, our findings showed that women with less education were older, have longer infertility duration.

Education is a vital determinant of fertility behavior and outcomes. The IVF treatment process is extremely complicated and requires efficient coordination of multiple links [20]. It is hypothesized that women with higher educational levels have a higher chance of avoiding mistakes in the IVF process. There have been several studies that have examined the association between maternal educational level and fertility [21–23]. Previous data from the demographic and health surveys confirms that higher education is associated with lower fertility [24]. The reason for reduced fertility is usually owned to birth postponement and the high opportunity cost of childbearing. More-educated women tend to marry later, have a week orientation towards having families [25]. However, the need and importance of ensuring fertility education is tailored to different women [26]. Less-educated women may be left ill-equipped to make informed choices about their reproductive lives and relationships [27]. In addition, women with higher levels of education have lower rates of depressive symptoms in IVF treatment [28]. This may offset the detrimental effect of postponing parenthood.

The association between live birth after IVF and maternal educational level has not been well investigated previously. It remains unclear whether women's educational level itself influences the clinical outcomes of IVF. One cohort study of 2569 women indicated that a woman's educational attainment was not associated with the likelihood of implantation failure, spontaneous abortion, or live birth [29], which is in accordance with our study. However, the women in this study were only divided into three educational categories: no college degree, college degree, and graduate attendance. The classification is fuzzy and does not apply to the current educational system.

In conclusion, our results demonstrated no relationship between maternal educational level and live birth in women undergoing IVF. Patients with less education are not less able to follow instructions for IVF protocols and potential preexisting discrimination or judgement towards these patients is neither ethical, nor supported by the data. In addition, physician and nurses should provide necessary education and counseling to patients undergoing IVF treatment despite their educational level. While the findings of this study are valuable in contributing towards the current understanding of the relationship between educational attainment and pregnancy outcome, further research needs to be undertaken before the results can be extrapolated to the general population.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10815-021-02345-4.

Declarations

Conflict of interest BWM reports grants from NHMRC, personal fees from ObsEva, personal fees from Merck KGaA, personal fees from Guerbet, personal fees from iGenomix, outside the submitted work. The other authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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