

ORIGINAL RESEARCH

# The Impact of Parental Preconception Body Mass Index on the Outcomes of in vitro Fertilization-Embryo Transfer and Newborns' Outcomes

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## ABSTRACT

**Objective** • Associations between parental pre-pregnancy BMI in IVF/ICSI fresh embryo transfer cycles and neonatal outcomes were investigated through a retrospective analysis.

**Methods** • A retrospective analysis of Couples who underwent IVF/ICSI fresh embryo transfer 1340 cycles from January 2019 to December 2021 was conducted in the Department of Reproductive Medicine of our hospital. Based on the preconception BMI of parents, they were divided into four groups: Group A (both father and mother with BMI < 25 kg/m<sup>2</sup>), Group B (father with BMI < 25 kg/m<sup>2</sup> and mother with BMI ≥ 25 kg/m<sup>2</sup>), Group C (father with BMI ≥ 25 kg/m<sup>2</sup> and mother with BMI < 25 kg/m<sup>2</sup>), and Group D (both father and mother with BMI ≥ 25 kg/m<sup>2</sup>). The differences in baseline characteristics, fertilization and embryo development, pregnancy outcomes, and neonatal outcomes were compared among the groups.

**Results** • In the IVF cycles, Group A had a higher rate of normal fertilization compared to three other groups, Group A is significantly higher than Group D, with statistical significance ( $P < .05$ ). In the ICSI cycles, there were no significant differences among the four groups regarding normal fertilization rate, day 3 high-quality embryo rate, blastocyst formation rate, and high blastocyst rate. Univariate and multivariate analysis results showed no significant differences in clinical pregnancy and live birth rates among the four groups. However, Group D had a significantly higher rate of preterm birth than other three groups, with statistical significance ( $P < .05$ ).

**Conclusion** • To achieve better clinical outcomes and neonatal outcomes, overweight or obese couples should lose weight before undergoing IVF/ICSI treatment. (*Altern Ther Health Med.* 2024;30(1):215-219).

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## INTRODUCTION

Overweight and obesity have become one of the most important health issues globally,<sup>1</sup> high blood pressure, cardiovascular disease and even cancer are increasing as a result of overweight and obesity. The population of obese and overweight individuals in our country is increasing yearly, more than 30 percent of adults are overweight. More and more studies have shown that obesity and overweight can affect human reproductive function, such as poor quality of oocytes and sperm, impaired endometrial receptivity, and even anovulation.<sup>2-5</sup> All will lead lower fertility rate and live birth rate. Body mass index (BMI) is currently used as an indicator to measure the degree of obesity, and many studies focus on

the independent or synergistic effects of preconception BMI of parents on the outcomes of assisted reproductive technologies (ART) and neonatal outcomes. However, the results of these studies are inconsistent. Some suggest that high BMI may be associated with poor ovarian response, fertilization, and lower clinical pregnancy and live birth rates in women.<sup>6-8</sup> Overweight or obese men have significantly reduced sperm concentration and total sperm count but increased DNA fragmentation index, leading to poor embryo quality and low pregnancy rates.<sup>9-11</sup> On the other hand, some studies have found no significant impact of BMI on the outcomes of couples that conceived via in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI).<sup>12,13</sup> It is possible that different criteria for inclusion of the population or different research methods may lead to differences in results. Therefore, this study aims to investigate the influence of preconception BMI of parents on the outcomes of couples that conceived via in vitro fertilization-embryo transfer and neonatal outcomes by analyzing relevant data from patients undergoing IVF/ICSI in our department.

In this study, we focused on outcomes included normal fertilization rate, blastocyst formation rate, high-quality blastocyst rate, clinical pregnancy rate, live birth rate, preterm

delivery rate, infant gender, low birth weight (birth weight < 2500 g), macrosomia (birth weight ≥ 4000 g). This study may further improve ART outcomes and neonatal health.

## MATERIALS AND METHODS

### Study Population

For retrospective analysis, we collected parents' data from our department who underwent IVF/ICSI-ET cycles from January 2019 to December 2021, with a total of 1340 cycles. The inclusion criteria were as follows: (1) female age <40 years, (2) IVF/ICSI fresh transfer cycles, excluding the following cases: (a) fewer than 5 retrieved oocytes, (b) couples with severe pre-existing complications such as hypertension or heart disease, (c) rescue ICSI or Half-ICSI cycles. Inclusion and exclusion criteria were minimize interferenced by other factors. Our hospital's Institutional Review Board approved the study protocol, the doctor explained the whole procedure to the patients clearly and all procedures were performed with the informed consent of the patients.

### BMI Groups

BMI was calculated as weight divided by height squared. According to the World Health Organization's classification, BMI ≥25 kg/m<sup>2</sup> was considered overweight, and BMI ≥30 kg/m<sup>2</sup> was considered obese. Due to the limited number of patients with BMI ≥30 kg/m<sup>2</sup> in this study, overweight and obese patients (BMI ≥25 kg/m<sup>2</sup>) were combined into one group for statistical analysis. Parental BMI before pregnancy was divided into four groups: Group A (both father and mother BMI <25 kg/m<sup>2</sup>), Group B (father BMI <25 kg/m<sup>2</sup>, mother BMI ≥25 kg/m<sup>2</sup>), Group C (father BMI ≥25 kg/m<sup>2</sup>, mother BMI <25 kg/m<sup>2</sup>), and Group D (both father and mother BMI ≥25 kg/m<sup>2</sup>).

### Study Methods

After oocyte retrieval, fertilization was achieved via either IVF or ICSI. On Day 1, fertilization was confirmed by observing the presence of pronuclei. High-quality cleavage-stage embryos were selected on Day 3 based on Peter's scoring system and cryopreserved. With the patients' informed consent, the remaining embryos were cultured to the blastocyst stage, and the formation of blastocysts was observed and recorded on Day 5 and Day 6. Blastocysts were graded using the Gardner scoring system.<sup>14</sup>

### Embryo Selection and Implantation

In our laboratory, fresh transfer cycles were conducted with high-quality embryos. For Day 3 transfers, we selected embryos that have reached the 7-9 cell stage, with fragmentation rates below 10% and even blastomeres. For Day 4 transfers, we chose embryos that had developed into compact morulas, and for Day 5 transfers, we selected blastocysts with a grade of 3BB or higher. The number of embryos transferred did not exceed two. We usually preferred single embryo for transfer, the type of embryo transferred was selected according to the patient's physical condition and the condition of the embryo.

**Table 1.** Characteristics of the included couples compared by maternal and paternal prepregnancy BMI

Variables	BMI				P value
	A (M&P < 25)	B (M ≥ 25 & P < 25)	C (M < 25 & P ≥ 25)	D (M & P ≥ 25)	
No. of cycles	402	162	533	243	
Female age(y)	32.37±3.47	32.44±3.55	33.03±3.60	32.91±3.22	.018
Male age(y)	33.79±4.17	33.77±4.40	34.53±4.77	34.03±3.89	.043
Female BMI(kg/m <sup>2</sup> )	21.12±2.12	27.73±2.49	21.53±1.97	28.43±2.75	<.001
Male BMI(kg/m <sup>2</sup> )	22.67±1.75	22.86±1.63	28.33±3.01	28.31±2.78	<.001
Type of infertility [n(%)]					.297
Primary	244(60.7)	95(58.6)	291(54.6)	142(58.4)	
Secondary	158(39.3)	67(41.4)	242(45.4)	101(41.6)	
Duration of infertility(y)	3.72±2.61	3.61±3.34	3.92±2.79	3.36±3.05	.098
Cause of infertility[n(%)]					.022
Male factor	64(15.9)	18(11.1)	57(10.7)	26(10.7)	
Female factor	241(60.0)	101(62.3)	313(58.7)	156(64.2)	
Both factor	69(17.2)	38(23.5)	110(20.6)	47(19.3)	
Unexplained	28(7.0)	5(3.1)	53(9.9)	14(5.8)	
ART method[n(%)]					.279
IVF	191(47.5)	65(40.1)	232(43.5)	100(41.2)	
ICSI	211(52.5)	97(59.9)	301(56.5)	143(58.8)	

**Abbreviations:** BMI, body mass index; M, maternal prepregnancy BMI; P, paternal prepregnancy BMI.

### Observation Indicators and Evaluation Criteria

On the 14th day after embryo transfer, blood β-human chorionic gonadotropin (β-HCG) levels were measured. If the test was positive, a transvaginal ultrasound was performed 4-5 weeks after transfer to confirm the presence of a gestational sac and fetal heartbeat, indicating clinical pregnancy. Progesterone support was continued until 10-12 weeks of pregnancy, and patients are followed up until delivery.

### Statistical analysis

Statistical analysis was conducted using Statistical Product and Service Solutions (SPSS) 25.0 software (IBM, Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation ( $\bar{x} \pm s$ ), and between-group comparisons were performed using analysis of variance (ANOVA). Categorical variables were presented as n (%), and between-group comparisons were made using non-parametric chi-square tests. Statistical significance was defined as  $P \leq .05$ . Multiple-level logistic regression was used to investigate the impact of parental prepregnancy BMI on clinical pregnancy, live birth, preterm birth, low birth weight (<2500 g), and macrosomia (>4000 g), with odds ratios (ORs) and 95% confidence intervals (CIs) reported.

## RESULT

Table 1 characteristics of the included couples compared by maternal and paternal prepregnancy BMI displayed the baseline characteristics of all couples included in comparing prepregnancy BMI. The age of both parents in Group C was significantly higher than in Group A, with a statistically significant difference ( $P < .05$ ). Among the causes of infertility, female factors were significantly higher than other factors ( $P < .05$ ). At the same time, there were no statistically significant differences in infertility types (primary and secondary infertility), duration of infertility, and assisted reproductive techniques (IVF and ICSI).

Embryo datas of the included couples compared by maternal and paternal prepregnancy BMI (Table 2) presented

the basic embryo information of all couples included. Subgroup analysis was conducted based on different assisted reproductive techniques, IVF or ICSI. In the IVF cycles, Group A had a significantly higher normal fertilization rate than Groups B, C, and D, with a statistically significant difference ( $P < .05$ ). The rates of high-quality Day-3 embryos, blastocyst formation, and high-quality blastocysts in Groups C and D were lower than in Group A, but the differences were not significant. In the ICSI cycles, there were no significant differences among the four groups regarding normal fertilization rate, high-quality Day-3 embryos, blastocyst formation rate, and high blastocyst rate.

Table 3 Outcomes presented the details of fresh embryo transfer cycles for all couples included. There were no statistically significant differences among the four groups in terms of the number and types of embryos transferred (cleavage-stage embryos, morulae, and blastocysts). The clinical pregnancy rate in Group D was slightly higher than in Group A, while Groups B and C had lower clinical pregnancy rates, but the differences were not significant ( $P = .602$ ). The four groups had no statistically significant differences in live birth rates ( $P = .503$ ). However, the preterm birth rate in Group D was significantly higher than in the other three groups, with a statistically significant difference ( $P < .05$ ).

Table 4 Neonatal outcome displayed the relevant outcomes of newborns after embryo transfer for all couples included. There were no statistically significant differences among the four groups regarding the rates of singleton births, twin births ( $P = .757$ ), and gender ratios of newborns ( $P = .955$ ). The proportion of low birth weight infants in Group A was lower than in Groups B, C, and D ( $P = .071$ ). In comparison, macrosomic infants in Group D was higher than in Groups A, B, and C ( $P = .970$ ), but these differences were not statistically significant.

Table 5 Associations between parental prepregnancy BMI and neonatal outcomes in multilevel logistic regression analyses presented the multiple logistic regression analysis results of the relationship between couple BMI and clinical outcomes and newborn outcomes. After adjusting for confounding factors, the results were consistent with the univariate analysis. Compared to Group A(11.4%), the preterm birth rate in Group D(17.9%) was significantly higher, with a statistically significant difference ( $P < .05$ ). Compared to normal-weight couples, overweight couples had a adjusted OR of 1.906 for preterm infants (95% CI).

These findings will be further discussed in terms of their implications for assisted reproductive technologies and neonatal outcomes.

## DISCUSSION

In today's society, an increasing number of couples are experiencing infertility due to overweight or obesity. Compared to natural conception, more couples are seeking assisted reproductive technology (ART). All of them are concerned about their offspring's success rate and health. This study explores the influence of parents' prepregnancy

**Table 2.** Embryo datas of the included couples compared by maternal and paternal prepregnancy BMI

Variables	BMI				P value
	A (M&P < 25)	B (M ≥ 25 & P < 25)	C (M < 25 & P ≥ 25)	D (M & P ≥ 25)	
IVF					
No. of cycles	189	64	229	98	
Normal fertilization rate(%)	75.68±22.25	73.66±22.87	73.58±22.73	71.24±26.78	.048
D3High-quality embryo rate(%)	34.67±23.82	30.13±24.69	33.30±27.37	32.99±30.81	.341
Blastocyst formation rate(%)	42.21±33.07	42.58±37.53	41.69±35.62	34.37±35.51	.304
High-quality blastocyst rate	33.98±37.72	34.53±41.78	33.79±39.91	31.88±40.15	.805
ICSI					
No. of cycles	210	91	299	142	
Normal fertilization rate(%)	92.34±16.08	93.24±16.05	91.81±15.84	95.15±13.17	.192
D3High-quality embryo rate(%)	37.66±20.24	42.09±22.237	36.72±20.35	33.94±26.50	.546
Blastocyst formation rate(%)	31.73±34.27	30.97±35.78	31.33±36.10	34.88±37.24	.794
High-quality blastocyst rate(%)	29.60±17.12	23.23±16.47	24.30±36.21	25.03±16.29	.558

**Table 3.** Outcomes of the included couples compared by maternal and paternal prepregnancy BMI with fresh embryo transfer cycle

Variables	BMI				P value
	A (M&P < 25)	B (M ≥ 25 & P < 25)	C (M < 25 & P ≥ 25)	D (M & P ≥ 25)	
No. of cycles	402	162	533	243	
Number of embryos transferred	1.71±0.46	1.71±0.47	1.74±0.46	1.68±0.47	.380
Embryo stage at transfer[n(%)]					.150
Cleavage embryo	317(78.9)	120(74.1)	415(77.9)	175(72.0)	
Morula	77(19.2)	40(24.7)	104(19.5)	64(26.3)	
Blastocyst	8(1.9)	2(1.2)	14(2.6)	4(1.6)	
clinical pregnancy rate[n(%)]	210(52.2)	79(48.8)	276(51.8)	134(55.1)	.602
Live birth rate[n(%)]	162(40.3)	59(36.4)	228(42.8)	103(42.4)	.503
Preterm birth rate(<37weeks)[n(%)]	24(11.4)	9(11.4)	32(11.6)	24(17.9)	.035

**Table 4.** Neonatal outcome of the included couples compared by maternal and paternal prepregnancy BMI

Variables	BMI				P value
	A (M&P < 25)	B (M ≥ 25 & P < 25)	C (M < 25 & P ≥ 25)	D (M & P ≥ 25)	
No. of clinical pregnancy cycles	210	79	276	134	
Singletons	119(56.7)	46(58.2)	181(63.1)	76(56.7)	.757
Twins	43(20.5)	13(16.5)	47(16.4)	27(20.1)	
Gender					
Boys	107(52.2)	35(48.6)	142(51.6)	69(53.1)	.955
Girls	98(47.8)	37(51.4)	133(48.4)	61(46.9)	
Low birth weight (< 2500 g)[n(%)]	33(16.1)	16(22.2)	61(22.2)	30(23.1)	.071
Fetal macrosomia (> 4000 g)[n(%)]	5(2.4)	2(2.8)	9(3.3)	5(3.8)	.970

**Table 5.** Associations between parental prepregnancy BMI and neonatal outcomes in multilevel logistic regression analyses[n(%)]

Variables	BMI				P value
	A (M&P < 25)	B (M ≥ 25 & P < 25)	C (M < 25 & P ≥ 25)	D (M & P ≥ 25)	
clinical pregnancy rate(%)	210(52.2)	79(48.8)	287(53.8)	134(55.1)	
aOR (95% CI)	REF	0.865	1.056	1.137	
P value		.446	.685	.442	
Live birth rate(%)	162(40.3)	59(36.4)	228(42.8)	103(42.4)	
aOR (95% CI)	REF	0.842	1.104	1.100	
P value		.379	.467	.571	
Preterm birthrate(%)	24(11.4)	9(11.4)	32(11.1)	24(17.9)	
aOR (95% CI)	REF	0.981	1.011	1.906	
P value		.962	.970	.036	
Low birth weight (<2500 g)	33(16.1)	16(22.2)	61(22.2)	30(23.1)	
aOR (95% CI)	REF	1.174	1.008	1.395	
P value		.675	.977	.303	
Fetal macrosomia (>4000 g)	7(3.4)	2(2.8)	9(3.3)	5(3.8)	
aOR (95% CI)	REF	0.744	1.026	1.194	
P value		.717	.960	.767	

**Note:** aOR, Odds ratio and 95% confidence interval (CI) were calculated from logistic regression models to reflect the associations between parental prepregnancy BMI and neonatal outcomes. Adjusted models are controlled for parental age, cause of infertility and duration of infertility. P value is based on multilevel logistic regression analysis.

BMI on the clinical outcomes of fresh embryo transfer cycles and the outcomes of newborns, aiming to provide effective recommendations for improving ART treatment outcomes.

Among this study's 1340 fresh embryo transfer cycles, there was no significant difference in fertilization rates between the four groups in the intracytoplasmic sperm injection (ICSI) cycles. This is consistent with previous studies, indicating that an increase in BMI for both men and women does not affect the treatment outcome of ICSI.<sup>15,16</sup> However, in the in vitro fertilization (IVF) cycles, Group A (both father and mother with BMI < 25 kg/m<sup>2</sup>) had the highest normal fertilization rate, significantly higher than the other groups ( $P < .05$ ). Furthermore, as BMI increased, Group D (both father and mother overweight or obese with BMI  $\geq$  25 kg/m<sup>2</sup>) had the lowest normal fertilization rate ( $P < .05$ ). Additionally, both in the IVF and ICSI cycles, the rates of good-quality day 3 embryos and blastocysts were higher in Group A compared to Group D, suggesting a possible association between the high prepregnancy BMI of parents and decreased embryo quality. There was no significant difference in clinical pregnancy rate and live birth rate among the four groups in this study, indicating that BMI does not affect embryo implantation. However, Group A (both father and mother with BMI < 25 kg/m<sup>2</sup>) had the lowest proportion of low birth weight infants, while Group D (both father and mother overweight or obese with BMI  $\geq$  25 kg/m<sup>2</sup>) had the highest proportion of macrosomia infants. This suggests that an increase in prepregnancy BMI of parents may increase the risk of low birth weight and macrosomia infants, similar to the findings of Wang et al.<sup>17,18</sup> However, this difference did not reach statistical significance, and further studies with larger sample sizes are needed to validate these results.

This study's univariate and multivariate analyses found that the preterm birth rate in Group D was significantly higher than the other three groups ( $P < .05$ ). The World Health Organization (WHO) defines preterm birth as delivery before 37 weeks of gestation. It has become a serious global public health issue, preterm birth is a major cause of neonatal and childhood mortality and morbidity, as well as an increased risk of neurodevelopmental disorders and chronic diseases in surviving preterm infants,<sup>19,20</sup> which imposes significant economic and emotional burdens on individuals, families, and countries.<sup>21</sup> Therefore, elucidating the factors influencing preterm birth is of great public health significance. Previous studies have explored the impact of high prepregnancy BMI on preterm birth,<sup>19,22,23</sup> and the research indicates that overweight women before natural conception or frozen embryo transfer (FET) are more likely to deliver preterm infants.<sup>24,25</sup> In 2016, Kawwass et al.<sup>26</sup> reported an increased risk of preterm birth associated with obesity in fresh autologous in vitro fertilization cycles.<sup>26</sup> The results indicate that couples with high prepregnancy BMI have a greater adverse impact on preterm birth in newborns compared to cases where only the mother has a high prepregnancy BMI. In obese women, excessive expansion of adipose tissue leads to elevated levels of serum-free fatty acids, accompanied by hyperinsulinemia,

inflammation, and oxidative stress, which directly or indirectly affect ovarian function and interfere with follicular development. In men, obesity disrupts the balance of reproductive hormones, interfering with sperm production.<sup>27,28</sup> Animal experiments have shown that both obese male and female mice, as well as cases where only one parent is obese, result in slower embryo development, reduced blastocyst count, and even mitochondrial damage.<sup>29,30</sup> Obesity is associated with various complications and comorbidities, and further research is needed to understand the mechanisms by which obesity in both parents negatively affects embryos.

Our research has some limitations, primarily a small sample size, which may prevent us from accurately assessing the impact of prepregnancy BMI increase in parents on neonatal outcomes. Additionally, BMI is measured based on patient's weight and height during the initial IVF/ICSI cycle, and we cannot control the weight gain of pregnant women during pregnancy, which may lead to inadequate or excessive maternal nutrition and increase the risk of preterm birth or macrosomia, potentially influencing the results with unknown confounding factors not included. We plan to increase further the number of couples enrolled for future research.

Prepregnancy body mass index (BMI) is a potentially modifiable and preventable lifestyle-related factor associated with neonatal outcomes.<sup>31</sup> Existing studies on the relationship between prepregnancy BMI and neonatal outcomes mainly focus on infants born from natural conception, with controversial and inconclusive results.<sup>24</sup> Liu et al. conducted a systematic review and meta-analysis, establishing the relationship between maternal BMI and neonatal outcomes in Chinese women, reporting an increased risk of preterm birth in overweight and obese women.<sup>32</sup> However, studies on the combined effect of prepregnancy BMI in both parents on ART and neonatal outcomes are rare. Our research indicates that parental prepregnancy overweight or obesity adversely affects fertilization rates in fresh embryo transfer cycles and neonatal outcomes. An increase in prepregnancy BMI in both parents indeed increases the risk of preterm birth. Therefore, this study provides a reference for further investigating the impact of prepregnancy BMI in both parents on ART neonatal outcomes. More studies about this issue must be conducted in the future.

Over-weight and obesity are more and more common in infertile couples. Based on the results of this study, overweight women should be informed about the risks during the perinatal period, and couples planning to conceive with the help of assisted reproductive technology are advised to control their weight before pregnancy. Optimizing BMI through dietary adjustments, physical exercise, and a healthy lifestyle can help improve embryo quality and neonatal outcomes. That may greatly improve effectiveness of ART treatment.

#### CONFLICT OF INTERESTS

The authors declared no conflict of interest.

#### AUTHOR CONTRIBUTIONS

SCT and YY designed the study and performed the experiments, XW and LL collected the data, CT and LL analyzed the data, CT and YY prepared the manuscript. All authors read and approved the final manuscript.



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