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Original Article

Correlation between body mass index of Chinese males and assisted reproductive technology outcome

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Abstract: Objective: To investigate the relationship between male's body mass index (BMI) and the outcome of assisted reproductive technology (ART). In this retrospective study, we analyzed the data from 729 cycles of female patients aged 38 years or less, with normal BMI and who received IVF treatments between January, 2013 and June, 2014. The patients were divided into normal weight (n = 358), overweight (n = 267), and obese (n = 104) groups according to the BMI of their male partners. Embryonic development and pregnancy outcomes in these three groups were compared. Results: With increasing BMI, fertilization rates decreased proportionately ($P < 0.05$); but embryonic cleavage rates and effective embryo rates were not significantly affected ($P > 0.05$). There was no significant difference in implantation rates, pregnancy rates, or early miscarriage rates ($P > 0.05$) among the three groups. Conclusions: High male BMI affects fertilization rate with ART; and we recommend that men of reproductive age adjust their lifestyles accordingly and make efforts to control their weight.

Keywords: Obesity, infertility, assisted reproductive technology, pregnancy outcome

Introduction

With the ongoing social and economic developments in society-as well as changes in the lifestyles of the general population-the incidence of obesity-related diseases is increasing year after year, thus bringing about a series of social, psychological, and physical health problems. The body mass index (BMI) is a person's weight in kilograms (kg) divided by his or her height in meters squared. The World Health Organization (WHO) recommends defining normal weight, overweight and obesity according to BMI. Recently, accumulating evidence has revealed that obesity seriously affects the fertility of women, including those who have undergone assisted reproductive technology (ART) [1]. However, the impact of obesity on male fertility must also not be ignored. Studies show that semen parameters decrease at different levels when male BMI increases, and that this is accompanied by changes in serum sex hormone concentrations [2]. At the same time, there has been growing concern over whether the BMIs of male partners are associated with ART outcomes [3-5]. However, the relationship between male body weight and ART outcomes in China has not been examined extensively. In this study, we analyzed the data from 729 initiated cycles of female patients who received *in-vitro* fertilization-embryo transfer (IVF-ET) therapy in our hospital, in order to investigate the influence of male BMI on the outcome of IVF-ET.

Materials and methods

Study sample

Retrospective data were collected from 729 cycles from 683 couples who participated in IVF at the ART unit of our hospital during January to December, 2013. The data analysis is based upon these cycles.

Inclusion criteria

To reduce the interference from variability in female partners on ovarian hyperstimulation and IVF-ET outcomes, we used the following criteria to select eligible female patients: 1) they were aged less than 38 years; 2) they had

Table 1. Descriptive characteristics of the study group

	Normal Weight (n = 358)	Overweight (n = 267)	Obesity (n = 104)
Male age (years)	33.1±4.6	33.6±4.7	33.5±5.0
Female age (years)	30.6±3.2	31.2±3.3	30.9±3.2
Female baseline FSH (IU/L)	8.1±6.8	8.0±4.2	7.6±1.7
E2 on HCG day (nmol/L)	15.2±8.3	13.8±7.7	15.1±8.0
Duration of infertility (years)	3.8±2.1	3.9±2.1	3.8±2.5
Female BMI	20.9±1.4	21.0±1.9	21.1±1.4
Gn dose (IU)	2067±719	2045±710	2065±719
Gn duration (days)	10.0±2.1	9.7±1.9	9.8±1.8
Number of oocytes	15.4±8.3	13.9±7.10	15.2±7.5
Number of implantation	1.9±0.2	2.0±0.2	2.0±0.2

Gn, gonadotropin.

undergone a long ovulation-induction program; 3) their infertility was due to tubal factors but not to endometriosis, polycystic ovary syndrome, hyperprolactinemia, thyroid dysfunction or other endocrine diseases; 4) both partners had normal chromosomes; and 5) female BMI was normal (18.5-23.9 kg/m^2) [6].

Inclusion criteria for the male patients were: 1) their reproductive organs developed normally, without a history of varicocele or cryptorchidism, no acute prostatitis, urethritis, or urinary tract infections; 2) they had no smoking history; and 3) their semen samples achieved the standard for IVF insemination after density gradient centrifugation.

Grouping

Height and weight were measured to determine BMI, with the patient dressed in light clothing with no shoes. Classification criteria recommended by the Cooperative Meta-Analysis Group of China Obesity Task Force were used to define overweight and obesity. Patients were divided into three groups according to their respective BMIs: normal (18.5-23.9 kg/m^2; a total of 358 cycles); overweight (24-27.9 kg/m^2; 267 cycles); and obese (≥ 28 kg/m^2; 104 cycles).

In-vitro fertilization and embryo culture

Each subject was treated with the standard long luteal-phase ovarian stimulation protocol [7]. Male semen samples were optimized by density gradient centrifugation on the day of oocyte retrieval. Up to 4 oocytes were added to every 100 μl medium under a dissection microscope, and inseminated with 60,000 motile spermatozoa. Normal fertilization was checked 16-18 hours after insemination, and the embryos were transferred after 72 hours. Embryos were scored by Veeck's embryo scoring system [8]. Grade I and II embryos were considered to be of high quality. Up to two high-quality embryos were transplanted. Ninety mg Crinone vaginal gel (Merck Serono, Switzerland) was administered per day for luteal phase support. The blood HCG level was measured two weeks after transplantation. Patients with a positive HCG result were followed two weeks later, and diagnosed with clinical pregnancy if a gestational sac was detected by ultrasonography, or a positive chorionic villus was seen in miscarriage tissue by pathological examination. Three months later, the pregnancy outcome was followed by phone. The following numbers were recorded: oocytes developing to M II, presence of male and female pronuclei (2PN), embryos having reached the cleavage stage, effective embryos, embryo transfer cycles and embryos per cycle. We then calculated the fertilization rate (2PN/M II), cleavage rate (cleavage number/2PN), and effective embryo rate (number of effective embryos/cleavage number). We also followed up with the status of pregnancy, the number of fetuses for each pregnancy, and the number of early miscarriages; and then calculated the ongoing pregnancy rate (pregnancy number/number of transplantation cycles), implantation rate (number of fetuses/transplanted embryos), and first trimester miscarriage rate (the number of early miscarriages/pregnancy number).

Statistical analyses

SPSS13.0 (Chicago, USA) was used to analyze the data. Data are represented as mean ± sd. One-way ANOVA was used to compare means among groups. After the means for fertility rate, embryonic cleavage rate and effective fertility rate were calculated, the relationships among the means of the BMI groups were analyzed using a simple linear regression model. χ^2 tests were used to compare the fertility rates, embryonic cleavage rates, effective embryo rates,

Table 2. Relationship between BMI groups and embryonic development by linear regression analysis

	Normal Weight (n = 358)	Overweight (n = 267)	Obesity (n = 104)	R^2	P
Fertility Rate (%)	78.8±20.1	77.9±22.1	77.1±23.9	0.998	0.022*
Embryonic Cleavage Rate (%)	96.2±8.3	95.4±10.7	95.7±7.6	0.382	0.575
Effective Embryo Rate (%)	53.0±24.9	50.2±24.3	57.1±23.0	0.348	0.598

*P < 0.05.

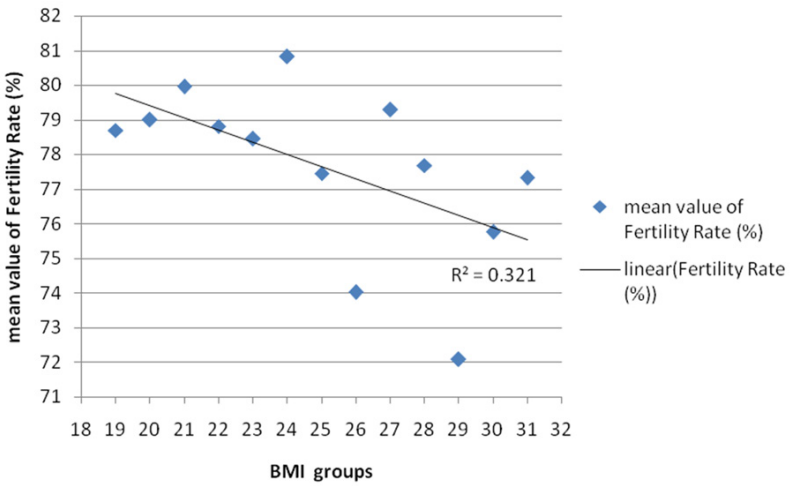

Figure 1. Relationship between BMI groups and mean vale of Fertility Rate (%); P < 0.05.

implantation rates, pregnancy rates and early miscarriage rates among groups. P < 0.05 was considered to be significant.

Results

General information

As shown in **Table 1**, there was no statistically significant difference in contributing female factors among normal, overweight and obese groups; including age, baseline FSH value, E2 on HCG day, duration of infertility, female BMI, ovarian stimulation by gonadotropin (Gn) dose and duration, or number of oocytes retrieved and embryos implanted.

Comparison of ART outcomes

As shown in **Table 2**, linear regression analyses showed that the mean of fertility rates decreased with the increase in BMI (P < 0.05) (**Figure 1**); and that embryonic cleavage rate and effective embryo rates were not related to BMI (P > 0.05). The fertility rates of the overweight and obese groups were significantly lower than those of the normal group; and although the fertility rate of the obese group tended to be lower than that of the overweight group, the difference was not statistically significant (P > 0.05). There were no significant differences (P > 0.05) in implantation rates, pregnancy rates or early miscarriage rates for either pregnancy outcome (P > 0.05) (**Table 3**).

Discussion

Unhealthy lifestyles-including excessive food intake, a high-fat diet, being sedentary, lacking physical activity, as well as certain genetic factors and metabolic disorders-can lead to energy imbalance, causing overweight and obesity. Elevated BMI reflects a poor lifestyle, which in turn may affect semen quality. BMI is a relatively simple indicator of obesity. According to the WHO's recommendations, normal adult BMI is between 20-25 kg/m^2, an individual with a BMI of 25-29.9 kg/m^2 is considered to be overweight, BMI ≥ 30 kg/m^2 is considered to be obese, and BMI ≥ 40 kg/m^2 is considered to be severely obese. Physical characteristics of the general Chinese population are different from those of Westerners, so we used the diagnostic criteria for Chinese adults for overweightness and obesity as recommended by the Cooperative Meta-Analysis Group of China Obesity Task Force.

Recent research has shown that with an increase in BMI, serum T levels decrease and E2 levels increase, while sperm concentration, motility and normal morphology rates decrease [9]. Research on ART outcomes is controversial. Some researchers believe that the increase in BMI may cause decreases in embryo quality

Table 3. Comparison of pregnancy outcomes

	Normal Weight (n = 358)	Overweight (n = 267)	Obesity (n = 104)
Fertility Rate (%)	79.0% (4346/5503)	76.9% (2853/3709)*	76.5% (1221/1597)*
Embryonic Cleavage Rate (%)	96.1% (4178/4346)	96.1% (2742/2853)	96.3% (1176/1221)
Effective Embryo Rate (%)	49.3% (2061/4178)	48.2% (1322/2742)	51.8% (609/1176)
Implantation Rate (%)	30.3% (318/1049)	31.5% (283/897)	28.5% (86/302)
Pregnancy Rate (%)	32.8% (245/748)	33.4% (213/637)	31.5% (67/213)
Early Miscarriage Rate (%)	5.7% (14/245)	8.5% (18/213)	9.0% (6/67)

*Compared with normal weight group; $P < 0.05$.

and pregnancy rates [3], while other researchers hypothesize that male BMI is not related to embryo fertility, cleavage or pregnancy rate [4]. We found in the aforementioned studies that the authors included both data from patients who had undergone IVF and those who had undergone intracytoplasmic sperm injection (ICSI); additionally, the authors' sample size was quite small. Clinical fertility rates with ICSI tend to be affected by each technician's technical skills. Thus, in our retrospective study we only included subjects who participated solely in IVF; and we also increased our sample size. Keltz [5] reported that overweight status of the male partner may cause impaired sperm-egg interaction after IVF but not after ICSI, and this is consistent with our findings that increased BMI is associated with decreased fertility rate after an IVF cycle. Sermondade et al. further showed that male BMI is not associated with sperm-zona pellucida-binding activity [10]. Compared to the overweight group, the fertility rate in the obese group did not decrease with increased BMI, which may be related to the body's adaptation to the overweight status, or homeostatic self-adjustment. Sperm-egg interaction and normal acrosin activity cannot guarantee a normal fertilization process; and the presence of antibodies (such as anti-zona pellucida antibodies, anti-nuclear membrane antibodies, *etc.*), the occurrence of the acrosome reaction, *etc.*, can all become obstacles to fertilization and cause fertilization failure. A clearer understanding of the detailed mechanism that regulates sperm-egg fertilization is warranted. Decreased fertilization rate in ART leads to a decreased ratio of effective embryo numbers to oocyte retrieval numbers, and decreased overall success rate. Thus, we speculate that the decreased natural conception rate of obese males is also related to the decline in their fertility. Sociological studies suggest that men generally gain weight after marriage, and progress quickly, because many men change their lifestyles after marriage; *e.g.*, they eat more regularly but exercise less. On the other hand, they may experience endocrine changes due to increased stress from family life. All of these factors can then lead to rapid weight gain, and it is in this stage of life where fertility is most desired. In fact, the natural conception rate in males tends to decline, which should also arouse concern regarding the association between obesity and fertility.

In our study, male BMI was not shown to be significantly associated with late-stage embryonic development, pregnancy rates or miscarriage rates. One possible reason is that as a factor that interferes with sperm quality, BMI does not affect all subjects to the same extent; as when undergoing IVF-ET, spermatozoa are processed and optimized, and this may eliminate affected sperm. Another reason may be that after sperm-egg interaction, impaired sperm could be repaired through the process of interactions with the oocyte [11]. Being carriers of embryonic development, females of course play much more important roles in determining pregnancy outcomes.

In conclusion, increased male BMI negatively affects sperm quality and fertility rates in ART. Thus, it is important to provide counseling services for obese males regarding weight control, so as to assist them in adjusting their lifestyles; and to control their weight through a series of interventions such as diet and exercise. These recommendations are significant with respect to their physical and mental health, and will help to increase both natural conception and ART fertility rates.

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Disclosure of conflict of interest

None.

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