Obesity and adverse pregnancy outcomes in older patients with decreased ovarian reserve: a retrospective single-centre study

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Research

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Title page

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Abstract

Background: In recent years, infertility has increased in older women with decreased ovarian reserve (DOR). Studies have shown that women with DOR have fewer oocytes, which are poorer in quality, and have an increased risk of adverse pregnancy outcomes. Pre-pregnancy BMI is significantly correlated with many adverse pregnancy outcomes. Therefore, we conducted this study to explore the correlation between body mass index (BMI) and abortion and live birth in older patients with DOR.

Methods: The clinical data of 2052 older women with infertility and DOR

admitted to the Reproductive Medicine Center of the First Affiliated Hospital of Zhengzhou University from August 2009 to May 2018 were analysed retrospectively. Patients were divided into underweight (BMI < 18.5 kg/m^2; n = 56), normal weight (18.5 kg/m^2 ≤ BMI < 24 kg/m^2; n = 1389), overweight (24 kg/m^2 ≤ BMI < 28 kg/m^2; n = 527) and obese (BMI ⩾ 28 kg/m^2; n = 80). We compared the pregnancy outcomes of patients in each group.

Results: Logistic regression analysis showed that being overweight or obese were independent risk factors for miscarriage (P < 0.05) and protection factors for live births (P < 0.05). Being underweight was a protective factor for live births (P < 0.05).

Conclusions: The abortion and live birth rates in older infertile women with DOR are correlated with BMI. Higher BMI was associated with higher abortion rates and lower live birth rates. Being underweight also correlated with the live birth rate. Therefore, to improve pregnancy outcomes, we suggest that older patients with DOR may benefit from maintaining a normal weight before seeking fertility treatments.

Keywords: diminished ovarian reserve; body mass index; miscarriage; live birth rate

Background

Ovarian reserve is the capacity for growth and development of follicles in the female ovarian cortex and the ability to form fertilised oocytes. Diminished ovarian reserve (DOR) is a common endocrine disease in women of childbearing age and

refers to the decline in the number and quality of oocytes, ovulation disorders, endocrine disorders, and infertility due to factors such as age, metabolism, genetics, autoimmunity, iatrogenicity, toxicity, and infection. In the process of assisted reproductive technology (ART), DOR is characterised by poor drug response, few eggs, low number of high-quality embryos, high rate of cycle cancellation, and low clinical pregnancy rate [1].

Studies have shown that pre-pregnancy BMI is significantly correlated with many adverse pregnancy outcomes, such as gestational diabetes mellitus (GDM), hypertensive disorders in pregnancy, premature birth, abnormal birth weight, and cesarean section [2,3]. However, there are currently insufficient data on the role of BMI in pregnancy outcomes in patients with decreased ovarian reserve. Therefore, we conducted this study to explore the relationship between BMI and pregnancy outcomes in patients with DOR to provide a reference for clinical practice.

Methods

1. Participant selection

We retrospectively analysed the clinical data of 2052 patients with decreased ovarian reserve who were treated for infertility at the Reproductive Medicine Center of the First Affiliated Hospital of Zhengzhou University from August 2009 to May 2018.

Inclusion criteria: (1) we used the 2015 U.S. Centers for Disease Control and Prevention DOR diagnostic criteria [4], which define DOR as the presence of

menstrual cramps and follicle stimulating hormone (FSH) > 10 IU/L, and/or anti-Mullerian hormone (AMH) < 1.0 ng/ml; (2) individuals above 35 years of age.

The exclusion criteria were as follows: (1) history of prior oocyte or sperm donation; (2) chromosomal abnormalities; (3) benign and malignant ovarian diseases; (4) sex hormone-dependent diseases, such as endometriosis, uterine fibroids, endometrial polyps, and pituitary tumours; (5) endocrine system diseases, such as diabetes, thyroid dysfunction, and hyperprolactinaemia; (6) oral administration of exogenous sex hormones or vitamin D within 3 months before consultation; (7) systemic diseases such as malignant tumours; (8) the absence of embryos for transfer or transplantation until the end of the follow-up period.

2. Research methods

1) Grouping: patients who met inclusion criteria were divided into four groups according to the Chinese Guidelines for Prevention of Overweight and Obesity in Adults: underweight (BMI < 18.5 kg/m^2; n = 56), normal weight (18.5 kg/m^2 ≤ BMI < 24 kg/m^2, n = 1389), overweight (24 kg/m^2 ≤ BMI < 28 kg/m^2, n =527), and obese (BMI ≥ 28 kg/m^2, n = 80).

2) Clinical data: clinical data were obtained from the clinical reproductive medicine management system or electronic medical record database of the Reproductive Medicine Center of the First Affiliated Hospital of Zhengzhou University. Data included age, BMI, menstrual cycle interval, antral follicle count (AFC) defined as number of antral follicles with a diameter of 2 mm-9 mm on ultrasound, infertility type, and number of previous IVF/ICSI cycles.

3) Specimen collection and laboratory tests: In the patient's natural physiological state, the second to fourth days of the menstrual cycle or menopause for more than 50 days (excluding early pregnancy and B-ultrasound monitoring of the ovaries and endometrium are consistent with anovulatory status), 3 ml of venous blood was drawn on an empty stomach, serum was collected by centrifugation, and electrochemiluminescence immunoassay kit (Roche, Germany) was used to detect serum basal luteinising hormone (bLH), basal follicle stimulating hormone (bFSH), and anti-Mullerian hormone (AMH) levels (inter- and intra-batch detection difference: < 5%).

4) ART protocol: a gonadotropin (Gn) releasing hormone (Gn) agonist was used to prevent a premature surge in luteinising hormone (LH), and Gn was used to stimulate follicular growth. When the largest follicle diameter was greater than 20 mm, and more than 2/3 of the total follicles were >16 mm. Human chorionic gonadotropin (hCG) was administered according to the serum FSH, LH, E2 and P levels. Ultrasound-guided egg retrieval was performed 36-38 hours later.

5) Outcome indicators: At 14 or 18 days after embryo transfer, serum β-hCG levels were measured to detect early pregnancy. Ultrasonography was performed 35 or 45 days after embryo transfer, and we diagnosed pregnancy clinically by the existence of an intrauterine pregnancy sac and a positive heartbeat. Miscarriage was defined as termination of pregnancy before 28 weeks' gestation with a foetal weight of less than 1000 g. Live birth was defined as at least one live birth after 24 weeks of pregnancy. We defined other outcomes as follows: implantation rate = number of

gestational sacs / number of embryos transferred × 100%; clinical pregnancy rate = number of clinical pregnancy cycles / total number of transplanted cycles × 100%; abortion rate = number of abortion cycles / total number of pregnancy cycles × 100%; and live birth rate = number of live birth cycles / total number of transplant cycles × 100%.

3. Statistical analysis was performed using SPSS 22.0 (IBM Corp., Armonk, NY, USA) statistical software for data analysis. Normally distributed data are expressed as mean ± standard deviation (x±s), one-way ANOVA was used for comparison between groups. Continuous variables with skewed distributions are represented as medians (interquartile ranges, IQR), and were compared using the Kruskal-Wallis test. Count data were expressed as rate (%), and the chi-square test was used to compare groups (X2). The difference of proportions between groups was compared using Bonferroni correction. Binary logistics regression was used to determine the correlation between BMI and pregnancy outcomes (abortion and live birth rates). The results are presented as the adjusted odds ratios (aORs) with the 95% confidence intervals (CIs). Statistical significance was set at $P < 0.05$.

Results

The retrospective analysis included 2052 patients, with 56 (2.7%), 1389 (67.7%), 527 (25.7%), and 80 (3.9%) patients classified as being underweight, normal weight, overweight, and obese, respectively. (Figure 1)

1. Baseline data

There were significant differences in male age, female age, menstrual cycle length, bFSH levels, bLH levels, AMH levels, and AFC among the different BMI classifications (all $P < 0.05$). Menstrual cycle length was directly proportionate to increased BMI. There were no significant differences in male BMI level, infertility diagnosis, and previous in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) attempts (all $P > 0.05$) (Table 1).

2. Analysis of patients' transplant status and assisted pregnancy results

The relationship between BMI and transplant and fertility outcomes of patients with reduced ovarian reserve was analysed. There was no significant correlation between BMI and initial Gn dose, Gn dosage, endometrial thickness on the day of HCG administration, number of retrieved oocytes, number of available embryos, number of embryos transferred, and embryo stage at transfer (all $P > 0.05$). However, we did find a significant correlation between BMI and the abortion rate ($P = 0.015$) and live birth rate ($P = 0.016$). There was no significant correlation between BMI and implantation rate, clinical pregnancy rate, number of live births, Cumulative clinical pregnancy rate (CCPR) or Cumulative live birth rate (CLBR) (all $P > 0.05$) (Table 2).

3. Analysis of factors affecting miscarriage

Using binary logistic regression to analyse related factors, we found that before adjusting for confounding factors, male age, female age, and being overweight were independent risk factors for miscarriage. After adjusting for male age, female age, menstrual cycle, bFSH, bLH, AMH, and AFC, only being overweight (adjusted odds ratio [aOR] = 2.41; 95% confidence interval [CI]: 1.20-4.83; $P = 0.013$) or obese (aOR

= 6.41; 95% CI: 1.38-29.70; P = 0.018) was independently associated with miscarriage, with the aOR value of the obesity group found to be several times that of the overweight group (Table 3; Figure 2A).

4. Analysis of factors correlated with abortion and live birth

Using binary logistic regression analysis, we found that male age, female age, and being overweight were independently associated with abortion before adjusting for confounding factors. After adjusting for male age, female age, menstrual cycle length, BMI, bFSH, bLH, AMH, and AFC, we found that factors such as being underweight (aOR = 0.15, 95% CI: 0.03-0.73; P = 0.019), overweight (aOR = 0.46, 95% CI: 0.23-0.91; P = 0.026), or being obese (aOR = 0.20; 95% CI: 0.04-0.91; P = 0.037) were independently protective in terms of the live birth rate. The impact of obesity far exceeded the impact of being overweight on the live birth rate (Table 4; Figure 2B).

Discussion

1. Reproductive difficulties in older patients with DOR

With the change in women's social roles and improved education levels, the global childbearing age has increased [5]. With the introduction of China's fertility policy, the proportion of older couples having children has increased significantly [6]. These factors have led to an increasing DOR detection rate. Patients with DOR have decreased fertility, by definition, and the incidence of infertility is increasing. In vitro fertilization/Intracytoplasmic sperm injection- embryo transplantation (IVF/ICSI-ET) has become an important method in the treatment of DOR-related infertility. Due to the

177 depletion of the ovarian pool in patients with DOR, the number and quality of oocytes
178 decreases, resulting in hormone secretion disorders [7]. In older patients with DOR
179 especially, cycle cancellation rates are high, pregnancy rates are low [8], and fertility
180 outcomes are poor. Nowadays, obesity is becoming a serious health problem [9]. The
181 proportion of obese women of childbearing age is increasing; this adversely affects
182 reproductive health and may lead to adverse pregnancy outcomes. Many studies
183 have shown that obesity significantly increases the risk of infertility and may cause
184 increased complications during pregnancy [10]. Therefore, it is necessary to
185 determine whether there is a correlation between BMI and pregnancy outcomes in
186 IVF/ICSI-ET in older patients with DOR in order to reduce their reproductive risk.
187 2. BMI and reproductive outcomes in older patients with DOR
188 Miscarriage is a common complication of pregnancy, and miscarriage after IVF
189 brings great pain to patients, especially DOR patients [11]. Previous studies have
190 described an increased rate of early miscarriage in obese patients, including
191 spontaneous and recurrent miscarriages [12-14]. Moreover, obese women have a
192 higher risk of pregnancy loss than overweight women, resulting in a lower live birth
193 rate among obese pregnant women [12,15]. However, some studies have not found a
194 clear correlation between increased BMI and abortion after in vitro fertilisation
195 [16,17]. According to literature reports, the incidence of spontaneous abortion is
196 approximately 15% in patients undergoing ART [18]. In the present study, the
197 miscarriage rate in patients with DOR receiving ART was 35.5%, which is
198 significantly higher than the average reported rate. In our statistical analysis, high

BMI was an independent risk factor for miscarriage in older patients with DOR; moreover, we found that the higher the BMI, the greater the risk of miscarriage (overweight [aOR = 2.41; 95% CI: 1.20-4.83] vs obesity [aOR = 6.41; 95% CI: 1.38-29.70]; both $P < 0.05$). Studies have found that compared to women with normal BMI, the live birth rate of women with increased BMI is significantly decreased [19,20]. Some scholars believe that there is no significant correlation between high BMI and live birth rate [21,22]. This study showed that there were significant differences in live birth rates among the different BMI groups. Our statistical analysis of factors affecting the live birth rate found that BMI was an independent factor in the live birth rate, that BMI affected the live birth rate of older women with DOR, and that the live birth rate decreased exponentially with an increase in BMI.

Many studies have confirmed that BMI affects embryo quality. Abnormal endocrine function and impaired mitochondrial function caused by abnormal fat content in obese patients， which reduces the quality of eggs and embryos [9,23], thus increasing the early abortion rate and reducing the live birth rate. In addition, synthetic leptin is a protein hormone secreted by adipose tissue that participates in the regulation of glucose, lipid, and energy metabolism [24]. Studies have shown that BMI can affect leptin receptor expression on endometrium during the secretory period, regulate uterine angiogenesis and implantation, and affect the pregnancy outcome of older patients with DOR. Changes in serum leptin are related to obesity and blastocyst implantation [25]. An increase in adipocyte-related cytokines, such as interleukin-6 and tumour necrosis factor, may pose potential risks for pregnancy [26].

Other studies have shown that obesity can cause ascending bacterial infections in the reproductive tract [27], change the susceptibility of pathogenic bacteria [19, 28], increase uterine cavity infections, increase the risk of miscarriage in older patients with DOR, and reduce the live birth rate. In addition, miscarriage in women with high BMI ($\geqslant$25 kg/m^2) is not mainly caused by chromosomal abnormalities in embryos [29]; BMI affects embryo quality and the maternal intrauterine environment through different mechanisms.

Being underweight is associated with negative pregnancy outcomes in patients receiving in vitro fertilisation through frozen-thawed embryo transfer [30]. In the present study, low BMI was correlated with live birth rate, which is consistent with previous findings. Decreased fertility in underweight women may be related to decreased leptin levels [30].

3. Lifestyle changes and pregnancy outcomes

Maternal obesity increases the risk of pregnancy complications such as GDM, gestational hypertension, and preeclampsia [31]. In addition, more than half of overweight and obese women gain more weight than recommended during pregnancy, which leads to an increased risk of perinatal complications and poor neonatal outcomes, and affects the health of the mother and future generations [32]. Studies have shown that female obesity is an independent risk factor in the cumulative live birth rate in the first complete ovarian stimulation cycle [33]. When the parents' BMI is high, the ratio of normal birth weight to macrosomia in single births increases [34]. In addition, maternal obesity is related to macrosomia, stillbirth, and

243 congenital abnormalities [31].

244 Lifestyle interventions can reduce BMI in obese women with infertility, including
245 older patients with DOR [35]. Therefore, for overweight and obese women who want
246 to conceive, it is strongly recommended that they implement lifestyle changes and
247 lose weight before starting infertility treatments. A decrease in body weight by 5%–
248 10% compared with baseline has been found to improve reproductive function
249 [36,37]. Studies have shown that infertile women can lose weight by changing their
250 lifestyle before conception and thus reduce the rate of spontaneous abortion [38, 39].
251 However, a disadvantage of losing weight through lifestyle changes is weight
252 rebound. Long-term behavioural counselling that provides diet or activity advice is
253 uncommon [36]. In addition, the impact of weight management on the outcome of
254 assisted reproduction remains uncertain [40].

255 The present study findings suggest that female obesity is an independent risk
256 factor for abortion in older patients with DOR, with greater risk in obese women than
257 in overweight women. In women with normal weight, BMI is an independent
258 protective factor in the live birth rate. Considering the difficulty experienced by
259 women with DOR in conceiving and remaining pregnant, and the high obesity rate in
260 older women, we recommend that women reduce their pre-pregnancy weight through
261 lifestyle changes.

262 4. Advantages and limitations

263 Our study presents a novel correlation of pregnancy outcomes in IVF/ICSI-ET
264 with BMI. We have attempted to control for confounding factors that affect pregnancy

outcomes as much as possible to improve the reliability of our results. Although we have reduced selection and confounding biases as much as possible, the present study is a retrospective study with inherent limitations. Our sample size for the underweight and obese patients is small. The study should be repeated with a larger sample size. In addition, this study is a single-centre study, and we only used the clinical data from recent transplant cycles of all older patients DOR in the same centre. Our study lacks some advantages of multi-centre research; however, single-centre research can arguably provide more consistent results by avoiding inconsistencies in surgical methods and laboratory conditions. Finally, we did not evaluate cumulative pregnancy outcomes or neonatal and obstetric outcomes, which may present opportunities for future research.

Conclusion

For infertile women > 35 years old with reduced ovarian reserve, pregnancy outcomes of IVF/ICSI-ET were correlated with BMI. We found that BMI above the normal range was correlated with an increased risk of miscarriage. Being underweight or overweight was also associated with the live birth rate. Obesity was more strongly associated with abortion and reduced live birth rate than being overweight. Our findings suggest that older patients with DOR who wish to conceive may benefit from maintaining a normal BMI to improve pregnancy outcomes during fertility treatment.

List of abbreviations

AFC, Antral follicular count

AMH, anti-Mullerian hormone

AOR, adjusted odds ratio

ART, assisted reproductive technology

bFSH, basal follicle stimulating hormone

bLH, basal luteinising hormone

BMI, body mass index

CCPR, Cumulative clinical pregnancy rate

CI, confidence interval

CLBR, Cumulative live birth rate

DOR, decreased ovarian reserve

FSH, Follicle-stimulating hormone

GDM, gestational diabetes mellitus

Gn, gonadotropin

hCG, human chorionic gonadotropin

ICSI, Intracytoplasmic sperm injection

IVF, In vitro fertilization

LH, luteinising hormone

OR, Odds ratio

Declarations

Ethics approval and consent to participate:

This research was approved by the Institutional Ethics Committee of the First Hospital of Zhengzhou University, and all patients signed an informed consent form. All methods were conducted in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used in the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

LFX: study design, analysis and interpretation of data, and drafting and revision of the manuscript; LJ: data collection; SH, SYC, DSJ, YQL: assessed the article; GYH: study conception and design. All authors approved the final article.

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Table 1: Baseline characteristics of women older than 35 years old with DOR

	Total	Underweight	Normal weight	Overweight	Obesity	*P*-value
Number of cycles	2052	56(2.7%)	1389(67.7%)	527(25.7%)	80(3.9%)	-
Male parameters						
Age(y) [ab]	40.6±4.3	40.0±4.3	40.6±4.3	41.1±4.4	40.2±4.0	0.001
BMI(kg/m^2)	25.4±3.0	24.7±3.2	25.3±3.0	25.4±3.1	26.0±3.1	0.187
Female parameters						
Age(y) [bcd]	39.9±3.0	38.7±2.5	39.7±2.9	40.5±3.2	40.3±3.3	< 0.001
Menstrual cycle(day) [e]	28.8±8.6	27.8±1.6	28.4±7.2	29.6±12.0	30.8±7.9	0.002
BMI [abcdef]	23.0±2.7	17.7±0.7	21.8±1.4	25.6±1.1	29.5±1.7	< 0.001
Baseline FSH(IU/L) [bcef]	11.4(10.1-13.9)	12.0(10.2-14.4)	11.6(10.2-14.3)	11.1(9.5-13.2)	10.4(8.1-14.3)	< 0.001
Baseline LH(IU/L) [cde]	5.3(3.8-6.9)	6.1(4.3-7.0)	5.5(4.0-7.2)	4.9(3.5-6.2)	4.2(2.9-5.9)	< 0.001
AMH (ng/mL)	0.7(0.5-0.9)	0.8(0.7-1.0)	0.7(0.5-0.9)	0.6(0.4-0.8)	0.6(0.4-0.9)	0.033
AFC(n) [b]	4.0(3.0-7.0)	6.0(3.0-7.0)	4.0(3.0-7.0)	4.0(2.0-6.0)	4.0(2.0-7.0)	0.010
Infertility diagnosis, n(%)						0.271[α]
Primary infertility	342(16.7%)	14(25.0%)	230(16.6%)	82(15.6%)	16(20.0%)	
Secondary infertility	1710(83.3%)	42(75.0%)	1159(83.4%)	445(84.4%)	64(80.0%)	
Previous IVF/ICSI attempts(n)	0.0(0.0-1.0)	0.0(0.0-1.0)	0.0(0.0-1.0)	0.0(0.0-1.0)	0.0(0.0-1.0)	0.411

"α" means chi-square test. Statistical significance is defined as P < 0.05.

Abbreviations: BMI=body mass index; FSH =follicle stimulating hormone; LH=luteinizing hormone; AMH=anti-Mullerian hormone; AFC=antral follicle count; IVF=in vitro fertilization; ICSI=intracytoplasmic sperm

Letter a, b, c, d, e, f indicated significant difference between groups.

[a]*P*: Comparison between Underweight and Normal weight patients.

[b]*P*: Comparison between Underweight and Overweight patients.

[c]*P*: Comparison between Underweight and Obese patients.

[d]*P*: Comparison between Normal weight and Overweight patients.

[e]*P*: Comparison between Normal weight and Obese patients.

[f]*P*: Comparison between Overweight and Obese patients.

Table 2: Treatment and pregnancy outcomes of DOR patients older than 35 years old

	Total	Underweight	Normal weight	Overweight	Obesity	*P*-value
Number of cycles	2052	56(2.7%)	1389(67.7%)	527(25.7%)	80(3.9%)	-
Gn initial dose(IU)	270.8±65.2	273.2±54.5	268.3±68.2	276.2±58.9	277.5±53.6	0.071
Gn dosage(IU)	3386.4±1210.2	3309.6±848.7	3338.2±1218.3	3484.8±1236.8	3631.1±1044.4	0.097
Endometrial thickness on HCG day(mm)	11.3±3.6	11.6±2.6	11.3±3.9	11.4±2.8	11.4±2.5	0.530
No. of retrieved oocytes(n)	4.0(2.0-6.0)	4.0(3.0-6.0)	4.0(2.0-6.0)	4.0(2.0-6.0)	4.0(2.3-6.0)	0.389
No. of available embryos(n)	4.0(2.0-6.0)	4.0(3.0-6.0)	4.0(2.0-6.0)	4.0(2.0-6.0)	4.0(2.3-6.0)	0.427
No. of embryos transferred(n)	2.0(1.0-2.0)	2.0(2.0-2.0)	2.0(1.0-2.0)	2.0(1.0-2.0)	2.0(1.0-2.0)	0.068
Embryo stage at transfer,n(%)						0.646$^{\beta}$
Cleavage stage	2024(98.6%)	55(98.2%)	1368(98.5%)	522(99.1%)	79(98.8%)	
Blastocyst stage	28(1.4%)	1(1.8%)	21(1.5%)	5(0.9%)	1(1.3%)	
Implantation rate, [%(n/N)]	16.3%(590/3613)	13.6%(15/110)	16.4%(402/2454)	16.1%(147/912)	19.0%(26/137)	0.644
Clinical pregnancy rate, [%(n/N)]	25.5%(524/2052)	25.0%(14/56)	25.8%(358/1389)	24.9%(131/527)	26.3%(21/80)	0.978
Miscarriage rate, [%(n/N)]^{bcde}	35.5%(186/524)	50%(7/14)	31.0%(111/358)	44.3%(58/131)	47.6%(10/21)	0.015$^{\beta}$
No. of live births(n)	1.0(0.0-1.0)	1.0(0.0-1.5)	1.0(1.0-1.0)	1.0(0.0-1.0)	1.0(0.8-1.3)	0.674
Live birth rate, [%(n/N)]^{cef}	61.5%(322/524)	35.7%(5/14)	65.6%(235/358)	54.2%(71/131)	52.4%(11/21)	0.016$^{\alpha}$
CCPR, [%(n/N)]	36.7%(753/2052)	35.7%(20/56)	37.3%(518/1389)	34.3%(181/527)	42.5%(34/80)	0.449$^{\alpha}$
CLBR, [%(n/N)]	57.6%(434/753)	45.0%(9/20)	59.7%(309/518)	54.1%(98/181)	52.9%(18/34)	0.336$^{\alpha}$

"α"means chi-square test. "β"means Fisher test. Statistical significance is defined as $P < 0.05$.

Abbreviations: Gn=gonadotropin; IU=international unit; HCG= human chorionic gonadotropin; CCPR=Cumulative clinical pregnancy rate; CLBR=Cumulative live birth rate.

[b]*P*: Comparison between Underweight and Overweight patients.

[c]*P*: Comparison between Underweight and Obese patients.

[d]*P*: Comparison between Normal weight and Overweight patients.

[e]*P*: Comparison between Normal weight and Obese patients.

[f]*P*: Comparison between Overweight and Obese patients.

Table 3: Logistic regression analysis of miscarriage related factors

	Univariable analysis		Multivariable analysis	
	Crude OR(95%CI)	*P*-value	Adjusted OR(95%CI)	*P*-value
Male age	1.05(1.01-1.09)	0.022	1.08(0.99-1.19)	0.097
Female age	1.19(1.10-1.29)	< 0.001	1.13(0.97-1.32)	0.115
Menstrual cycle	1.00(0.99-1.01)	0.924	1.00(0.98-1.02)	0.945
BMI				
Underweight	2.22(0.76-6.47)	0.145	2.67(0.53-13.47)	0.234
Normal weight	1*		1*	
Overweight	1.76(1.17-2.66)	0.007	2.41(1.20-4.83)	0.013
Obesity	2.02(0.83-4.88)	0.121	6.41(1.38-29.70)	0.018
Baseline FSH	1.03(0.99-1.07)	0.156	1.01(0.94-1.10)	0.729
Baseline LH	1.01(0.98-1.05)	0.422	1.03(0.99-1.07)	0.207
AMH	0.92(0.60-1.43)	0.718	0.91(0.46-1.80)	0.789
AFC	0.96(0.91-1.01)	0.142	0.99(0.87-1.13)	0.893

*This variable functions as an indicator. Other categories of the same variable were compared with it. Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval. Statistical significance is defined as $P < 0.05$.

Table 4: Logistic regression analysis of live birth related factors

	Univariable analysis		Multivariable analysis	
	Crude OR (95%CI)	*P*-value	Adjusted OR(95%CI)	*P*-value
Male age	1.05(1.01-1.09)	0.022	0.94(0.86-1.03)	0.153
Female age	1.19(1.10-1.29)	< 0.001	0.88(0.76-1.03)	0.106
Menstrual cycle	1.00(0.99-1.01)	0.924	1.00(0.98-1.02)	0.911
BMI				
Underweight	2.22(0.76-6.47)	0.145	0.15(0.03-0.73)	0.019
Normal weight	1*		1*	
Overweight	1.76(1.17-2.66)	0.007	0.46(0.23-0.91)	0.026
Obesity	2.02(0.83-4.88)	0.121	0.20(0.04-0.91)	0.037
Baseline FSH	1.03(0.99-1.07)	0.156	0.98(0.91-1.06)	0.682
Baseline LH	1.01(0.98-1.05)	0.422	0.97 (0.93-1.01)	0.179
AMH	0.92(0.60-1.43)	0.718	1.30(0.66-2.56)	0.453
AFC	0.96(0.91-1.01)	0.142	0.99(0.88-1.13)	0.928

*This variable functions as an indicator. Other categories of the same variable were compared with it. Abbreviations: OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval. Statistical significance is defined as $P < 0.05$.

Figure1: Flow chart of the patients enrolled and the grouping

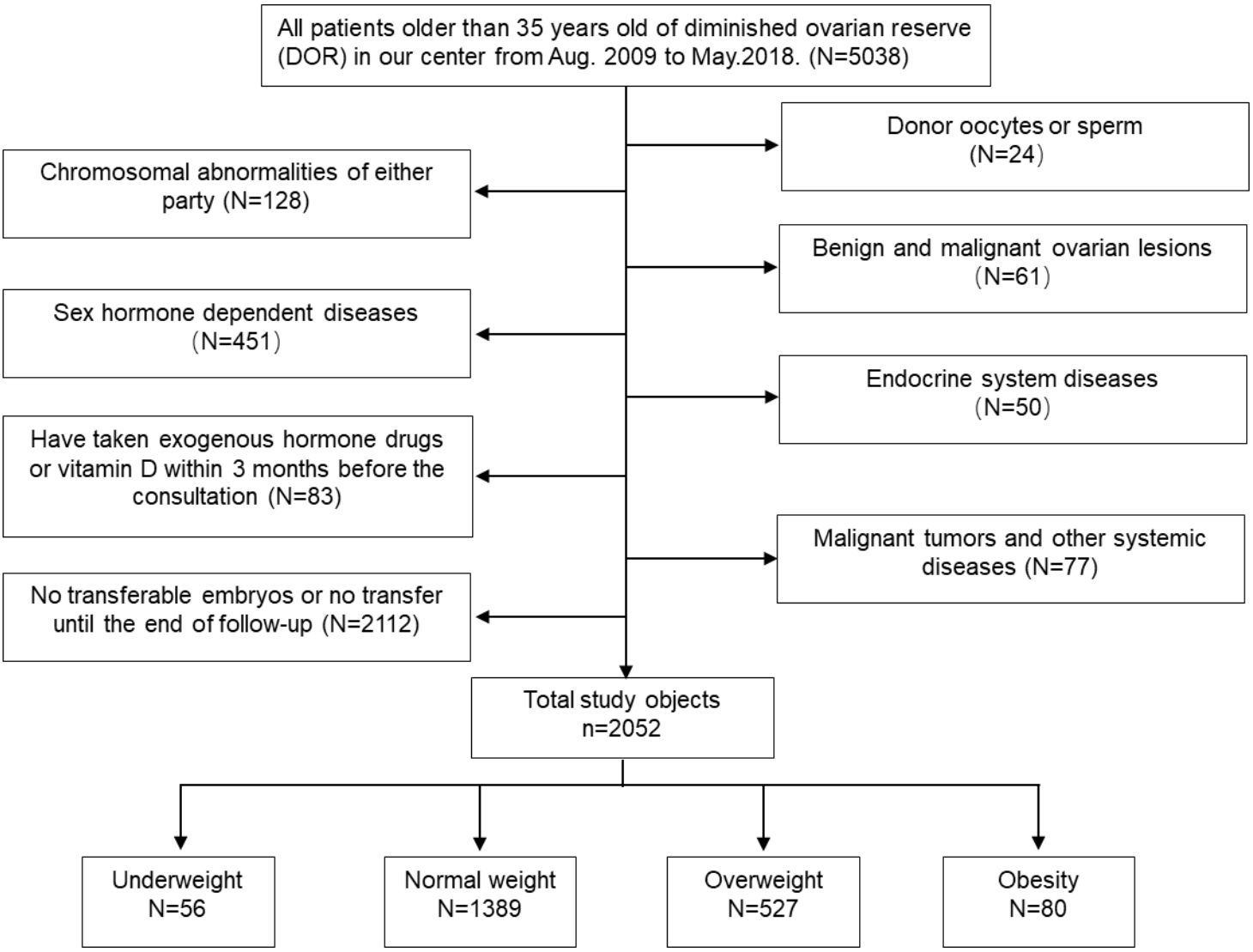

Figure2: Key factors affecting the miscarriage rate and the live birth rate