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INFLUENCE OF COUPLE BODY MASS INDICES ON THE TREATMENT OUTCOMES AND EXPECTED NEONATAL BODY WEIGHTS ASSOCIATED WITH INTRACYTOPLASMIC SPERM INJECTION CYCLES

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ABSTRACT

Aim of Study: To investigate the effects of Egyptian couples' body mass indices (BMIs) on the outcomes of intracytoplasmic sperm injection (ICSI) and the clinical parameters of their neonates. **Design:** Prospective double-centric randomized study which randomized by computer. **Setting:** International Islamic Center for Research and Population Studies Al-Azhar University and private infertility center from November 1, 2012 to December 31, 2015. **Main Outcome Measure(s):** Live birth was the main treatment outcome while the main outcome for the neonates was neonatal body weight (NBW). **Result(s):** With adjusting of confounders, this study showed that in ICIS cycles, couples with a female BMI $\geq$ 25 kg/m^2 had a significantly higher odds of abortion and a significantly lower odds of live birth than couples with both male and female BMI < 25 Kg/m^2. The neonatal body weight of singletons was significantly higher when their parents' BMIs were greater; while, there are no significant differences were obtained in the NBWs of twins. **Conclusion:** Live births conceived via ICSI were negatively affected by increased maternal BMI while not affected by paternal BMI. The neonatal body weights of singletons increased with paternal BMI which did not significantly affect the NBWs of twins.

KEYWORDS: Body mass index, Intracytoplasmic sperm injection, Live birth, Neonatal birth weight.

INTRODUCTION

Obesity is a seriously growing worldwide problem. The World Health Organization (WHO) determine that 1.5 billion people worldwide are overweight (body mass index (BMI) between 25 and 30 kg /m^2) and 400 million are obese (BMI > 30kg/m^2) and it's rates in the developing world have tripled in the last decades.[1] The proportion of obesity is increasing, and the average age of obesity is decreasing.[2]

Many recent studies have shown that obesity has adverse effects on the human reproductive system, leading to endocrine disorders, anovulation, and decreases in the oocyte quality.[3] Obesity also has adverse effect on endometrial receptivity and the female reproductive environment, thereby undermining fertility and increasing the rates of spontaneous abortion.[4] In addition, obesity has been associated with decreased semen quality and altered serum hormones in men.[5]

Prepregnancy associated with maternal obesity also negatively affects neonates and has an incidence of macrosomia.[6] Different opinions exist regarding whether obesity negatively affects the treatment outcomes of assisted reproduction technology (ART). Some studies have shown that females with higher body mass indices (BMIs) have poorer outcomes than normal-weight females undergoing IVF,[7] whereas the results from another retrospective study of approximately 880 females undergoing IVF or IVF/ intracytoplasmic sperm injection (ICSI) did not find any significance between female BMI and the clinical outcome[8] and the same results also were found in studies of the association between male BMI and IVF/ICSI outcomes.[9]

Most studies of BMI and ART outcomes have only investigated one of couple BMIs.[10] In addition, most studies have considered the live birth rate only as the treatment outcome and have not examined newly born outcomes.[11] So, this study determined both effects of Egyptian couples' BMIs on the treatment outcomes and the clinical parameters of the neonates conceived via ICSI in addition to live birth rate.

MATERIALS AND METHODS

Sample

Egyptian couples were treated with their fresh ICSI cycles of autologous oocytes at an International Islamic Center for Population Studies and Research Al-Azhar University and private infertility ICSI center, from November 1, 2012 to December 31, 2015 were studied. The couples had undergone fresh ICSI treatment with transferred day-3 or day-5 embryos, and couple BMI and

their neonatal information and follow-up records for the cycles were available.

The patients in this study were treated following different protocols for controlled ovarian stimulation (COS), such as long protocol, short protocol, and the minimal dose stimulation protocol. The selected protocol was based on the female serum hormone levels, age and ovarian function. Oral contraceptive pills, such as Marvelon (N.V. Organon) were given for some patients as a pretreatment to ICSI before COS.

Transvaginal ultrasonography was done to observe the growth of follicles during COS, and the serum E2, LH, FSH, and P levels over the cycle were monitored. The patients received a SC injection of 5,000-10,000 IU hCG (Chorionic Gonadotrophin for Injection), when they had at least three follicles with a mean diameter ≥ 20mm, and ultrasound-guided transvaginal oocyte retrieval was performed 36 hours later.

At 4-6 hours after oocyte retrieval, fertilization methods (ICSI) were performed depending on the sperm parameters. Then one to three high-quality day-3 or day-5 embryos were transferred into the uterus. Progesterone injection and dydrogesterone tablets (Abbott Laboratories) were given for luteal support beginning on the day of the oocyte retrieval.

The serum β-hCG concentration after 14 days of ET was measured. An abdominal ultrasound examination on day 35 after ET was necessary. Clinical pregnancy was determined when we found a gestation sac and a fetal heartbeat in the uterus upon ultrasonography, and the abdominal ultrasound examination was reviewed at 4th month of pregnancy.

Live birth was defined as at least one live infant born at 22-42 weeks' gestation among couples who obtained a clinical pregnancy. Clinical outcomes of ICSI cycles, the clinical parameters of the neonates and live birth rates were recorded via a telephone follow-up assessment.

Data

A total of 2240 cycles were included in this study. All of the cycles were classified into four groups, depending on the patients' BMIs and based on World Health Organization obesity standards (group A: both male and female BMIs were <25 kg/m^2; group B: female BMI ≥ 25 kg/m^2 and male BMI <25 kg/m^2; group C: female BMI <25 kg/m^2 and male BMI ≥ 25 kg/m^2; and group D: both male and female BMIs were ≥ 25 kg/m^2). Group A was considered as a control group.

Outcomes

The main pregnancy outcome was live birth. Secondary outcomes of treatment included clinical pregnancy, abortion, female and male ages, duration of infertility, basic serum FSH levels, diminished ovarian reserve, polycystic ovary syndrome (PCOS), duration of stimulation, total gonadotropin dose, number of oocytes retrieved, number of embryos cleaved, number of available embryos, endometrial thickness on the ET day, and number of embryos transferred.

Regarding the neonates, gestational age and neonatal birth weight (NBW) were recorded and also for the following indicators: premature birth, low birth weight (i.e., NBW <2,500 g), and fetal macrosomia (i.e., NBW >4,000 g) were evaluated.

Statistical Analyses

Continuous variables, such as NBW, are presented as the mean ± SD and compared via analysis of variance, whereas categorical variables, such as live birth and abortion, are presented as frequencies and percentages and compared via the C2 test. It was considered $P < 0.05$ had a significant difference.

SPSS 17.0 (IBM) was used for analyses of ICSI cycles in this study. The patients' characteristics, clinical outcomes and clinical parameter of the neonates were compared among groups A, B, C, and D. Group A was considered as the control group.

A multilevel logistic regression was used to evaluate the relationship between the couples' BMIs and their pregnancy outcomes, which was expressed using an OR with 95% confidence intervals (CIs). The analyses were adjusted for female age, male age, duration of infertility, basic serum FSH and PCOS.

RESULTS

A total of 2240 ICSI cycles were included in this study with a live birth rate 45.5% from which 1020 live birth (640 singletons, 380 twins) born from the included cycles with available NBW information were included in this study.

Table 1 shows the clinical parameters of the treatment cycles compared by couple BMIs. The average female age, average male age, duration of infertility, and basic serum FSH level were significantly higher in groups B, C, and D compared with group A ($P < 0.001$). The rate of PCOS was significantly higher in groups B and D compared with group A ($P < 0.05$). However, no significant differences were occurred in decreased ovarian reserve ($P > 0.05$).

Table 2 shows no significant differences were observed in the number of embryos transferred and endometrial thickness on day of ET between the four groups for ICSI cycles outcomes according to couple BMIs (P>.05). A significantly higher total gonadotropin dose were in groups B,C and D (P< .05). Groups B and D were significantly higher in oocytes retrieved, embryos cleaved, and available embryos than group A (P< 0.05). Table (3) & figure (1) show that the clinical pregnancy and live birth rates were significantly lower in groups B, C, and D compared with group A, whereas the abortion

rates of these groups were higher (P<.05). Group D had the lowest clinical pregnancy rate (46%).

Table 4 shows the multilevel logistic regression results for the couple BMIs and the pregnancy outcomes. After adjusting for female age, male age, duration of infertility, basic serum FSH level, endometrial thickness on the ET day, and PCOS, this study showed that groups B and D had a significantly higher odds of abortion (group B: OR 1.74, 95% CI 1.32-2.21; group D: OR 1.39, 95% CI 1.02-1.65) and a significantly lower odds of live birth (group B: OR 0.73, 95% CI 0.64-0.89; group D: OR 0.76, 95% CI 0.68-0.87) compared with group A in ICSI cycles.

Tables 5 and 6 show the clinical outcomes for singletons and twins conceived via ICSI. This study analyzed the data of 640 singleton newborns and 380 twin newborns. For the singletons, neonatal body weight as in figure (2) and fetal macrosomia rates were significantly higher for groups B, C, and D compared with group A (P< 0.05). Group D had the highest fetal macrosomia rate (18.7%). Significant differences were observed between the four groups as regard to premature birth rate among the parents who underwent ICSI (P< .05). The highest premature birth rate (13.7%) was associated with group B. For the twin births, groups B and D had a significantly higher premature birth rate than group A (48% and 40%, respectively; P < 0.05). None of the variables significantly differed among the four groups undergoing ICSI treatment (P > 0.05).

Table 1: Clinical parameters of patients by couple BMIs.

	Group A (male BMI < 25 kg/m^2, female BMI < 25 kg/m^2)	Group B (male BMI < 25 kg/m^2, female BMI ≥25 kg/m^2)	Group C (male BMI ≥ 25 kg/m^2, female BMI <25 kg/m^2)	Group D (male BMI ≥ 25 kg/m^2, female BMI ≥25 kg/m^2)	P value
N (total n=2240)	958	196	848	238	
Female age (y)	29.91±4.90	31.22±5.31	31.80±4.90	32.63±5.24	0.000
Male age (y)	30.32±5.20	32.17±5.41	33.18±5.56	33.88±5.66	0.000
Duration of infertility (y)	4.91±3.30	5.09±3.65	4.67±3.48	5.38±4.14	0.034
Basic serum FSH (mIU/mL)	6.68±2.90	6.93±3.30	6.83±4.22	7.45±3.31	0.027
Infertility diagnosis:					
PCO	29(30.2)	15(7.6)	22(2.5)	20(8.4)	0.000
Diminished ovarian reserve	3(0.3)	1(0.5)	6(0.7)	1(0.8)	0.692

Table 2: Effect of stimulation on ICSI cycle according to female and male BMIs.

	Group A (male BMI < 25 kg/m2, female BMI < 25 kg/m^2)	Group B (male BMI < 25 kg/m2, female BMI ≥25 kg/m^2)	Group C (male BMI ≥ 25 kg/m2, female BMI <25 kg/m^2)	Group D (male BMI ≥ 25 kg/m2, female BMI ≥25 kg/m^2)	P value
Total gonadotropin does (IU)	2099±830.31	2533.80±990.51	2384.77±965.21	2580.90±975.36	0.000
No. of oocytes retrieved	10.45±5.52	12.57±5.93	10.09±5.51	12.81±5.72	0.000
No. of embryos cleaved	7.98±5.01	8.93±5.39	7.78±4.88	9.01±5.21	0.001
No. of available embryos	5.09±3.45	5.99±3.53	5.01±3.31	5.87±4.53	0.000
No. of embryos transferred	1.91±0.45	1.89±0.48	1.92±0.44	1.91±0.48	0.861
Endometrial thickness on ET day (mm)	11.82±2.61	11.68±1.91	11.61±1.88	11.89±1.87	0.148

Table 3: Clinical outcomes of ICSI cycles according to female and male BMIs.

	Group A (male BMI < 25 kg/m2, female BMI < 25 kg/m^2)	Group B (male BMI < 25 kg/m2, female BMI ≥25 kg/m^2)	Group C (male BMI ≥ 25 kg/m2, female BMI <25 kg/m^2)	Group D (male BMI ≥ 25 kg/m2, female BMI ≥25 kg/m^2)	P value
Clinical pregnancy 507(52.9)	507(52.9)	92(46.9)	432(50.9)	108(46.0)	0.127
Abortion	71(7.4)	25(12.7)	59(6.9)	26(10.9)	0.016
Live birth	402(41.9)	62(31.6)	334(39.3)	78(32.7)	0.008

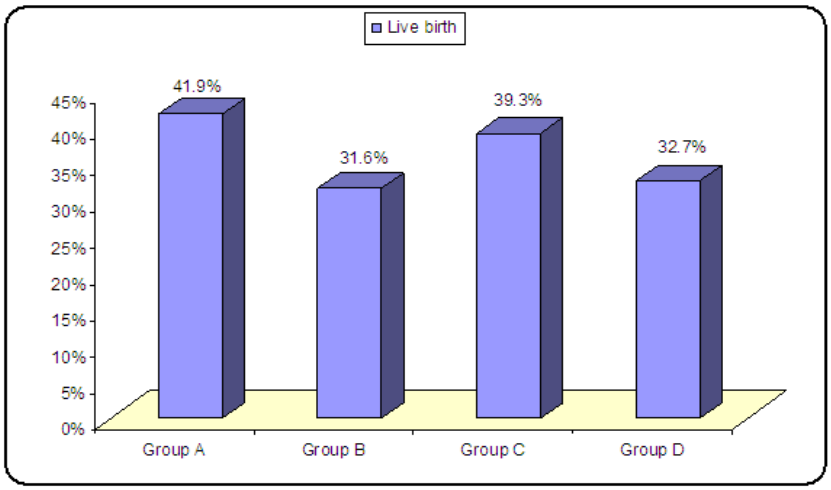

Figure 1: Clinical outcomes of ICSI cycles according to live birth.

Table 4: Multilevel logistic regression of female and male BMI on the pregnancy outcome associated with ICSI cycles.

	Group A (male BMI < 25 kg/m2, female BMI < 25 kg/m^2)	Group B (male BMI < 25 kg/m2, female BMI ≥25 kg/m^2)	Group C (male BMI ≥ 25 kg/m2, female BMI <25 kg/m^2)	Group D (male BMI ≥ 25 kg/m2, female BMI ≥25 kg/m^2)
Clinical pregnancy 507(52.9)	Reference	0.93(0.78-1.14)	0.92(0.89-1.03)	0.87(0.76-1.04)
Abortion	Reference	1.74(1.32-2.21)	1.09(0.89-1.27)	1.39(1.02-1.65)
Live birth	Reference	0.73(0.64-0.89)	0.97(0.88-1.13)	0.76(0.68-0.87)

Table 5: Clinical characteristics of singleton newborns conceived via ICSI.

	Group A (male BMI < 25 kg/m2, female BMI < 25 kg/m^2)	Group B (male BMI < 25 kg/m2, female BMI ≥25 kg/m^2)	Group C (male BMI ≥ 25 kg/m2, female BMI <25 kg/m^2)	Group D (male BMI ≥ 25 kg/m2, female BMI ≥25 kg/m^2)	P value
Number	287	51	238	64	
Gestational age (wk)	38.45±1.59	38.63±2.01	38.74±1.66	38.71±1.82	0.237
Premature birth	14(4.9)	8(15.69)	14(5.9)	5(78.)	0.033
NBW (g)	3370.45±514.00	3495.17±616.00	3470.94±655.32	35200.82±594.44	0.000
Low birth weight	9(3.1)	3(5.9)	8(3.4)	2(3.1)	0.796
Fetal macrosomia	30(10.4)	13(25.49)	33(13.9)	12(18.7)	0.019

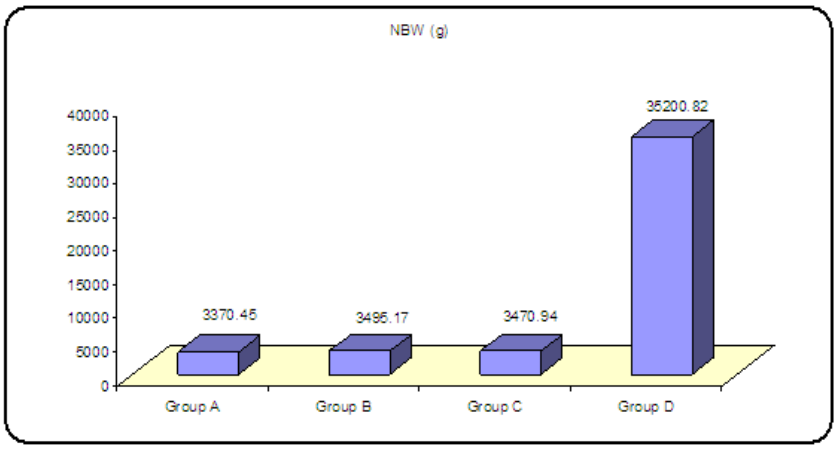

Figure 2: Neonatal body weight parameters of singletons.

Table 6: Clinical characteristics of twin newborns conceived via ICSI.

	Group A (male BMI < 25 kg/m2, female BMI < 25 kg/m^2)	Group B (male BMI < 25 kg/m2, female BMI ≥25 kg/m$_2$)	Group C (male BMI ≥ 25 kg/m2, female BMI <25 kg/m^2)	Group D (male BMI ≥ 25 kg/m2, female BMI ≥25 kg/m^2)	P value
Number	177	25	143	35	
Gestational age (wk)	36.70±2.03	36.40±2.33	36.62±2.12	36.52±2.19	0.897
Premature birth	60(33.9)	16(64.0)	47(32.9)	14(40.0)	0.021
NBW (g)	2515.64±487.13	2598.90±465.15	2557.87±415.22	2610.23±509.12	0.602
Low birth weight	67(37.8)	10(40.0)	55(38.4)	11(31.4)	0.695
Fetal macrosomia	2(1.1)	1(4.0)	2(1.3)	1(2.8)	0.799

DISCUSSION

The World Health Organization (WHO) determine that 400 million people world wide are obese (BMI > 30kg/m^2) and it's rates in the developing world have tripled.[1] So, the aim of this study was the investigation of the effects of Egyptian couples' body mass indices (BMIs) on the outcomes of intracytoplasmic sperm injection (ICSI) and the clinical parameters of their neonates.

The results of this study indicated that increases in female BMI adversely affected treatment outcomes, leading to decreases in live birth rates and an increase in the abortion rates during ICSI cycles. After adjusting of couple ages, duration of infertility, basic serum FSH level and PCOS, increasing in BMI gains increasing in NBW and fetal macrosomia rates of singletons during ICSI cycles while, couples' BMIs ≥ 25 kg/m^2 were not associated with this increasing in NBW of twins. This study showed significant differences in the number oocytes retrieved, embryos cleaved, available embryos, and pregnancy outcomes among the four groups.

After adjusting for possible confounding factors, couples with female BMIs ≥ 25 kg/m^2 had significantly higher odds of abortion and significantly lower odds of live birth than controls (i.e., both women and men with BMIs <25 kg/m^2), which suggests that increased female BMI negatively affects the live birth rates associated with ICSI and leads to an increased abortion rate. These findings were supported by most studies. A retrospective study of 4583 patients undergoing their first IVF/ICSI cycle showed that the live birth rate decreased dramatically as female BMI increased.[11] Another study of 582 patients undergoing IVF/ICSI in France also showed that the risk of abortion increased with increasing female BMI.[12] Studies have suggested that alterations in metabolism, endocrine factors, and the endometrium among obese women are associated with poor outcomes.[13,14] Physical activity before ART treatment helps obese patients achieve better pregnancy outcomes.[15]

The live birth rate was the major pregnancy outcome of this study. The results showed that female BMIs ≥ 25 kg/m^2 were negatively correlated with the live birth rate after ICSI cycles compared with group A (group B: OR 0.73, 95% CI 0.64-0.89; group D: OR 0.76, 95% CI 0.68-0.87).

A study of 8,457 women undergoing IVF in the Netherlands indicated that the live birth rate among women with BMIs > 27 kg/m^2 was significantly lower than that of normal-weight women (OR 0.67, 95% CI 0.48-0.94).[7] For the men, a study of 612 couples undergoing ART did not find significant differences in the clinical pregnancy or live birth rates compared with their male counterparts' BMI undergoing IVF and ICSI cycles[9] while another study in Denmark also showed that increases in couples BMIs negatively affect the live birth rate after ART.[10]

Other study of 951 IVF/ICSI cycles in Canada found that the live birth rate did not significantly differ among, overweight or obese women.[8]

While when determine the relationship between male BMI and ART outcomes, a study of 310 IVF cases indicated that increased BMI among men can adversely affect the pregnancy rate by influencing the IVF embryo quality.[16] However, these studies were limited by their small sample sizes and for IVF cycles only not for both ICSI and IVF cycles. Also another studies have not found that increased female or male BMI negatively affects pregnancy outcomes via ICSI so, a retrospective study of 288 ART cycles suggested that ICSI may overcome the adverse impact of obesity on sperm- egg fusion[17,18] but, these studies were limited by their small sample sizes.

The NBW and the rate of macrosomia of the singletons conceived were significantly higher when their parents' BMIs were greater. The results of spontaneous pregnancy studies have also found that prepregnancy obesity is related to fetal macrosomia and premature birth.[19]

No differences in NBW or fetal macrosomia were observed among twins. So, my study analyzed the correlation between couples' BMIs ICSI treatment outcomes in Egyptian patients for the first time but some studies have shown that women of different races had significantly different live birth rates after ART treatment.[20]

In conclusion, the results of this study indicate that increased female BMIs negatively affect the outcomes of ICSI, leading to a lower live birth rate and a higher

abortion rate. So, female BMI > 25 kg/m^2 was a dependent risk factor for abortion and stillbirth. The fetal macrosomia rate of singletons increased with increasing couple BMIs for ICSI cycles. Increases in the couples' BMIs did not significantly affect the birth weights of twins. Therefore, appropriate interventions for obese couples, such as improved lifestyles and weight-loss exercises, might help to improve outcomes and to avoid limitations as the lack of records on maternal health conditions during pregnancy and some confounders such as pregnancy hypertension syndrome, gestational diabetes, and pregnancy with cardiac disease, which have adverse effects on the fetus, more NBW studies must be performed in the future.

REFERENCES

1. Hossain P, kawar B, El-Nahas M. Obesity and diabetes in the developing world – a growing challenge. N Engl/ Med, 2007; 356: 213-215.
2. Kong AP, Choi KC, Ho CS, Chan MH, Ozaki R, Chan CW, et al. Associations of uric acid and gamma-glutamyltransferase (GGT) with obesity and components of metabolic syndrome in children and adolescents. Pediatr Obes, 2013; 8: 351-7.
3. Aladashvili-Chikvaidze N, Kristesashvili J, Gegechkori M. Types of reproductive disorders in underweight and overweight young females and correlations of respective hormonal changes with BMI. Iran J Reprod Med, 2015; 13: 135-40.
4. Dag ZO, Dilbaz B. Impact of obesity on infertility in women. J Turk Ger Gynecol Assoc, 2015; 16: 111-7.
5. Davidson LM, Millar K, Jones C, Fatum M, Coward K. Deleterious effects of obesity upon the hormonal and molecular mechanisms controlling spermatogenesis and male fertility. Hum Fertil (Camb), 2015; 18: 184-93.
6. Sharifzadeh F, Kashanian M, Jouhari S, Sheikhansari N. Relationship between pre-pregnancy maternal BMI with spontaneous preterm delivery and birth weight. J Obstet Gynaecol, 2015; 35: 354-7.
7. Lintsen AM, Pasker-de Jong PC, de Boer EJ, Burger CW, Jansen CA, Braat DD, et al. Effects of subfertility cause, smoking and bodyweight on the success rate of ICSI. Hum Reprod, 2005; 20: 1867-75.
8. Legge A, Bouzayen R, Hamilton L, Young D. The impact of maternal body mass index on in vitro fertilization outcomes. J Obstet Gynaecol Can, 2014; 36: 613-9.
9. Thomsen L, Humaidan P, Bungum L, Bungum M. The impact of male overweight on semen quality and outcome of assisted reproduction. Asian J Androl, 2014; 16: 749-54.
10. Petersen GL, Schmidt L, Pinborg A, Kamper-Jorgensen M. The influence of couple body mass index on live births after assisted reproductive technology treatment: a nationwide register-based cohort study. Fertil Steril, 2013; 99: 1654-62.
11. Moragianni VA, Jones SM, Ryley DA. The effect of body mass index on the outcomes of first assisted reproductive technology cycles. Fertil Steril, 2012; 98: 102-8.
12. Caillon H, FreourT, Bach-Ngohou K, ColombelA, Denis MG, Barriere P, et al. Effects of female increased body mass index on in vitro fertilization and intracytoplasmic sperm injection cycles outcome. Obes Res Clin Pract, 2015; 9: 382-8.
13. Bellver J, Melo MA, Bosch E, Serra V, Remohi J, Pellicer A. Obesity and poor reproductive outcome: the potential role of the endometrium. Fertil Steril, 2007; 88: 446-51.
14. Budak E, Fernandez M, Bellver J, Cervero A, Simon C, Pellicer A. Interactions of the hormones leptin, ghrelin, adiponectin, resistin, and PYY3-36 with the reproductive system. Fertil Steril, 2006; 85: 1563-81.
15. Palomba S, Falbo A, Valli B, Morini D, Villani MT, Nicoli A, et al. Physical activity before IVF and ICSI cycles in infertile obese women: an observational cohort study. Reprod Biomed Online, 2014; 29: 72-9.
16. Anifandis G, Dafopoulos K, Messini CI, Polyzos N, Messinis IE. The BMI of men and not sperm parameters impact on embryo quality and the IVF outcome. Andrology, 2013; 1: 85-9.
17. Akpinar F, Demir B, Dilbaz S, Kaplanoglu I, Dilbaz B. Obesity is not associated with the poor pregnancy outcome following intracytoplasmic sperm injection in women with polycystic ovary syndrome. J Turk Ger Gynecol Assoc, 2014; 15: 144-8.
18. Keltz J, Zapantis A, Jindal S, Lieman H, Santoro N, Polotsky A. Overweight men: clinical pregnancy after ART is decreased in IVF but not in ICSI cycles. J Assist Reprod Genet, 2010; 27: 539-44.
19. Galliano D, Bellver J. Female obesity: short- and long-term consequences on the offspring. Gynecol Endocrinol, 2013; 29: 626-31.
20. Luke B, Brown MB, Stern JE, Missmer SA, Fujimoto VY, Leach R. Racial and ethnic disparities in assisted reproductive technology pregnancy and live birth rates within body mass index categories. Fertil Steril, 2011; 95: 1661-6.