International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Bahgat NA. Int J Reprod Contracept Obstet Gynecol. 2022 Oct;11(10):2600-2604
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20222356

Original Research Article

Relation between maternal body mass index and laboratory outcome in normal responder young patients undergoing intracytoplasmic sperm injection cycles

Nagwan Ahmed Bahgat[1]*

Department of Obstetrics and Gynecology, Mansoura University Hospital, Mansoura Faculty of Medicine, Egypt

Received: 21 August 2022
Accepted: 05 September 2022

***Correspondence:**
Dr. Nagwan Ahmed Bahgat,
E-mail: nagwanivm@yahoo.com

ABSTRACT

Background: A lot of studies conducted evaluating the effect of maternal weight on the In Vito Fertilization (IVF) cycles outcome, the results of these studies were conflicting.
Methods: We conducted retrospective cohort study on young normal responding patients attending the clinic for fertility treatment. Patients divided in to three group according to their body mass index (BMI). All patients had intra cytoplasmic sperm injection cycle with antagonist protocol. The IVF laboratory outcome was calculated and compared between the three groups.
Results: The intracytoplasmic sperm injection cycles laboratory outcome was evaluated in the three groups of patients. No significant difference was found between the laboratory out come in the three group.
Conclusions: We concluded that in absence of sever major factor for infertility, maternal BMI has no effect on the laboratory outcome of intra cytoplasmic sperm injection cycles.

Keywords: Fertility, Obesity, Normal responder, BMI

INTRODUCTION

Obesity is a worldwide problem, its incidence in the reproductive age women have been increased dramatically. Obesity have been defined by having high body mass index (BMI) and according to WHO classification BMI between 19-24.9 kg/m^2 is normal weight, between 25-29.9 kg/m^2 considered overweight, between 30-34.9 kg/m^2 considered class 1 obesity, between 35-39.9 kg/m^2 class 2 obesity, and 40 kg/m^2 and above considered class 3 obesity.[1] The association between obesity and low fertility have been proven through a lot of studies. Women affected by obesity have three-fold increased incidence of infertility with lower birth rate and increased miscarriage rate this is beside perinatal maternal and fetal morbidity associated with obesity.[2-4] The mechanism by which obesity affects the fertility was through its effect on the hypothalamic-pituitary-ovarian axis, androgen: estrogen ratio disturbance, increased insulin resistance, all these factors could affect ovulation and disturb folliculogensis.[5] Obesity increases the oxidative stress and inflammatory markers in the follicular fluid which leads to negative effect on the cumulus cells gene expression, spindle formation, chromosome segregation that may influence oocytes developmental competence.[6-8] Recently Obese patients with infertility have access to assisted reproduction technology (ART), and with the increased number of assisted reproduction cycles in obese patients the doctors started to experience difficulties in their In Vito Fertilization (IVF) cycles starting from increased doses of gonadotrophins, prolonged period of stimulation, and with morbid obesity came the problems of difficult anesthesia and difficult oocyte retrieval, increased rate of surgical trauma and infections.[9] From this points studies started to investigate and report the risk factors and draw backs of IVF cycles in patients with high BMI. Some studies reported the need for more doses of gonadotrophins,

prolonged stimulation, increased cycle cancellation rate, fewer oocyte retrieval, lower rates of embryo transfer, and in other study found that the obesity affects the embryo development in a negative way that the embryos of obese women were slower than embryos of normal weight patients in the time laps study of the embryos, the negative effect of obesity on the endometrial tissue and endometrial receptivity have also been noticed with a lower pregnancy, lower live birth rates and higher miscarriage rates.[10-14] However, in other studies they failed to find relation between obesity and ART outcome up to the ploidy status of the embryos.[15-17]

In IVF cycles oocyte performance and embryo quality could be assessed in the laboratory and in clinical way. Laboratory assessment includes the number and quality of oocytes collected, its maturation, fertilization, cleavage, and blastocyst formation rate and availability of good quality embryos and recently blastocyst available for transfer or biopsy and preimplantation genetic study.[18]

Although some studies have linked obesity to poor ovarian reserve, low oocyte quality and decreased IVF success rate but no one could confirm this relation however negative reproductive outcome in IVF cycles could be attributed to other factors such as maternal age, negative sperm parameters or genetic and environmental factors that leads to poor ovarian reserve such as exposure to chemotherapy, radiotherapy, endometriosis and/ surgeries.[19]

We conducted this study to find out the effect of high BMI on the performance of oocytes collected and quality of embryos resulted from these oocytes. We eliminated the age factor, sever sperm parameters, and poor responders to concentrate on the effect of obesity on the outcome of Intracytoplasmic sperm injection cycles.

METHODS

Our study is a retrospective cohort study done in large private IVF center (Fakih IVF center) in Abu Dhabi, United Arab Emirates. Patient attended the clinic in period between January 2019 and December 2020. The study included analysis of IVF cycles outcome in normal responder patients with AMH between 1.1 to less than 5 ng/ml with an age of 35 years old or less. The patients included in the study were divided in to 3 groups. The first group with normal BMI 19-24.9, the second group with BMI between 25-29.9, the third group included patients with BMI more than 30 kg/m^2.

The patient included in the study were patients with primary and secondary infertility with all fertility work up done and underwent ICSI cycles. Exclusion criteria included patients with well-known chromosomal abnormalities, couples who had sever male factor, PCOS. Before the start of the cycle patient weight and BMI calculation done and documented. All patients went through ICSI cycle with antagonist protocol for ovarian stimulation. Patients attended the clinic in their second or third day of period. Trans- vaginal scan done to ensure endometrial shedding, normal ovaries, antral follicle count. Gonadotrophins started at a dose between 225-450 units daily of recombinant FSH then to start on gonadotropin releasing hormone antagonist on day 6 of the cycle. Follow up by transvaginal ultrasound after one week. decision for trigger and oocyte retrieval 36 hours after the trigger shot. The trigger used was recombinant human chorionic gonadotrophins 500 IU.

Presurgical checkup done before the day of egg retrieval. on the day of oocyte retrieval patient came fasting for 8 hours, under conscious sedation and under ultrasound guidance oocyte collection will be done. Oocytes collected were handled to the IVF laboratory. Oocytes were washed with global w/HEPES media (Cooper surgical group, USA) then cultured in global fertilization medium (Cooper surgical group, USA), oocytes were stripped of their cumulus cells after one hour of retrieval in hyaluronidase medium (80 IU/ml: Cooper surgical, USA). All mature oocytes were inseminated by ICSI under magnification of 40 times using an inverted microscope (Olympus 1X-73, Japan) and micromanipulator (Narishigi, Japan).

After ICSI procedure, oocytes were cultured separately in pre-equilibrated droplets of 25 ml of global total LP medium (Cooper surgical group, USA) overlaid by mineral oil (LIGHT OIL, Cooper surgical, USA). All embryos were incubated in ESCO bench top at 37^0 C under atmosphere of 6.0% CO_2, 6.0% O_2, 88% N_2, and PH of 7.28 to 7.32.

Assessment of quality of embryo and culture till day 5 blastocysts grading to be done and decision for biopsy, freezing and or transfer according to the quality of the embryos available.

Statistical analysis

Patients to be divided in to 3 groups according to their BMI: group 1 with BMI between19 and 24.9, group 2 with BMI between 25-29.9, group 3 with MBI above 30 kg/m^2. The outcome of ICSI cycle will be evaluated including number of oocytes collected, number of mature oocytes, rate of maturation, number of fertilized oocytes, rate of maturation, number of cleaved oocytes, rate of cleavage, number of blastocyst and blastocyte rate. Data will be analyzed with MS excel and will be presented in numbers, percentages, mean ± standard deviation the difference well be calculated between the three groups using the chi square and one way ANOVA test to find the significant deference, P value is considered significant when<0.05.

RESULTS

This study included 339 ICSI cycle in 339 patients, 119 (35.10%) patients in group 1 with BMI between 19-24.9 kg/m^2, 113 (33.33%) patients in group 2 with BMI between 25-29.9 kg/m^2, and group three included 107 (31.56%) patients with BMI above 30 kg/m^2 with mean

age of 30±3.85 for all cases and 30±4.40 for group one, 31±3.45 for group 2 and 30±3.87 for group 3. The mean BMI was 27.65±6.32 for all cases, 22.57±1.64 for group 1, 27.2±1.24 for group 2 and 34.31±6.82 for group 3. The mean AMH was 2.84±1.02, with 2.91±1.10 and 2.83±0.98 for group 2 and 2.74±0.96 for group 3.

In our study we found that the mean number of oocytes collected was 14±6.55 for group 1, 14±8.13 for group 2 and 15±7.46 for group 3. The p=0.846 which was non-significant deference. The mean number of mature oocytes was 11±5.28 for group 1, 11±6.72 for group 2, 12±5.98 for group 3 and p=0.701 showing that the deference was not significant. The mean number of fertilized oocytes was 8±4.26 for group one, 9±6.02 for group 2, 9±5.06 for group 3 with p=0.806 which is non-significant value.

The mean number of cleaved oocytes was 8±4.26 for group 1, 8±5.96 for group 2, 9±4.96 for group 3 and this was non-significant difference as the p=0.841. the mean number of blastocysts was 4±2.76 for group 1, 5±3.31 for group 2, 5±3.57 for group 3 and the p=0.0838 indicated non-significant difference.

In another way, the rate of cycle outcome was calculated and compared between the three groups, we found that the maturation rate was 78.09% for group 1,79.87% for group 2.80.78% for group 3 and the p=0.361. the fertilization rate was 77.84% for group 1, 75.49% for group 2, 74.09% for group 3 and p=0.268. cleavage rate per mature oocytes was 75.52% for group 1,73.75% for group 2,71.47% for group 3 with p=0.278. the cleavage rate per fertilized oocyte was 96.61% for group 1, 96.88 %for group 2, 96.78% for group 3 with p=0.978.

The blastocyst rate per mature oocytes was 46.7% for group 1, 43.37% for group 2, 40.82% for group 3 and p=0.157. the blastocyst rate per fertilized oocytes was 59.28% for group 1, 57.41% for group 2, 55.10% for group 3 and the p=0.499. the blastocyst rate per cleaved embryo was 61.39% in group 1, 59.51% in group 2, 57.51% in group 3 and the p=0.477

Table 1: Criteria of the patients involved on the study.

Variables	All	Group 1	Group 2	Group 3
Numbers	339	119	113	107
Age (Years)	30±3.85	30±4.40	31±3.45	30±3.87
BMI (kg/m^2)	27.65±6.32	22.57±1.64	27.20±1.24	34.31±6.82
AMH	2.84±1.02	2.91±1.10	2.83±0.98	2.74±0.96

Table 2: ICSI cycles outcome.

Variables	All	Group1	Group2	Group3	P value
Oocyte number	4851-14±7.39	1646-14±6.55	1596-14±8.13	1609-15±7.46	0.846
Mature oocytes	3819-11±6.03	1263-11±5.28	1275-11±6.72	1281-12±5.98	0.701
Fertilized oocytes	2913-9±5.14	972-8±4.26	973-9±6.02	968-9±5.06	0.806
Cleaved oocytes	2815-8±5.09	941-8±4.26	944-8±5.96	930-9±4.96	0.841
Blastocyst	1621-5±3.35	578-4±2.76	518-5±3.31	525-5±3.57	0.0838

Table 3: Rate of ICSI cycles outcome.

Variables	Group 1 (%)	Group 2 (%)	Group 3 (%)	P value
Maturation rate	78.09	79.87	80.75	0.361
Fertilization rate	77.84	75.49	74.09	0.268
Cleavage rate/mature oocytes	75.52	73.75	71.47	0.278
Cleavage rate /fertilized oocyte	96.61	96.88	96.78	0.978
Blastocyst rate/mature oocyte	46.70	43.37	40.82	0.157
Blastocyst rate /fertilized oocyte	59.28	57.41	55.10	0.499
Blastocyst rate /cleaved oocytes	61.39	59.51	57.71	0.477

DISCUSSION

Several factors could affect the IVF cycles outcome, these factors included the ovarian reserve, maternal age, previous failure, chromosomal abnormalities, and sperm parameters. Other factors were suggested by the clinicians in the IVF field to affect the outcome either in the laboratory aspect or clinical aspect such as some patients' characteristics as BMI, vitamin D level, thyroid situation. Stimulation protocols, skills of the clinician and embryologists handling the gametes, media and incubators, preimplantation genetic screening or no, day of embryo biopsy if ever to be done, day of embryo transfer, frozen or fresh cycles for transfer, the experience of the clinician for the transfer and the luteal phase support. With the advancement of IVF and ICSI and the possibility to offer them to patients with high BMI, several studies were done to find out the effect of BMI on the outcome of IVF

cycle and the results were conflicting, in our study we conducted the research after almost standardization of all other factors that could affect the laboratory IVF outcome such as the age, AMH, the protocol of stimulation, exclusion of sever sperm parameters to concentrate only on the BMI. We found that regarding the patients with high BMI (group 3) had lower number of oocytes aspirated in relation to other two groups, but the difference was not significant. Also, no significant difference was found in the mean number of mature oocytes collected, fertilized oocytes, cleaved embryos and blastocyst available for transfer or biopsy. this conclusion is with agreement of study done Batolacc et al which concluded that the high BMI do not affect the embryo performance and morphology but on the same time obesity affected the speed of embryo development in time laps assessment of the embryos, and they suggested that patients with high BMI had increased levels of insulin, inflammatory markers, triglycerides, non-esterified fatty acids in the follicular fluid of oocytes from those patients and these factors could cause lipotoxicity that affects the mitochondrial distribution and increases the level of reactive oxygen species that damages the organelles in the oocytes. our finding was also in agreement with studies done by Metwally et al who found no effect of obesity on embryo quality and Shah et al who failed to find negative effect of obesity on oocyte and embryo quality.[20-22] On the other hand, Matalliokis et al found that patients with high BMI had lower number of follicles, oocytes collected and embryos available than patients with normal BMI which could be explained by the lipotoxcity mechanism of oocyte damage as before.[23] In our study we did not only calculate the mean number of the product of ICSI, but the rate of the outcome and we did not find any significant difference in the maturation, fertilization, cleavage, and blastocyst rate which support our previous conclusion that the effect of high BMI on the laboratory outcome of IVF cycles is non-significant in cases of young aged normal responding patients. Which was supported by the studies mentioned before who failed to find relation between high BMI and oocyte and embryo performance, more over recent study conducted in 2021 by Stovezky et al failed to demonstrate any relation between high BMI and the ploidy status of the embryos.[24] On the other hand, and from clinical point of view some studies found that the implantation and miscarriage rate in IVF cycles were affected by patients BMI in a negative way which could be explained by the effect on endometrial receptivity as seen in a study by Bellver et al on recipient patients of donated oocytes found that the pregnancy and implantation rates were reduced in patients with high BMI which was justified by the effect of obesity on endometrial receptivity, but in a study by Sarais et al found that no difference noticed in the pregnancy rate among different BMI groups in spite noticing the increased miscarriage rate in patients with high BMI.[10,25] On the other hand, and in a study by Enarsson et al about the effect of weight reduction on the IVF outcome found that weight loss for patients with high BMI may not rectify the outcome in IVF cycles.[26]

CONCLUSION

in our study we could not find any significant effect of high BMI on the IVF cycle outcome in the laboratory performance of the oocytes and the embryos up to the blastocyst stage. Larger studies are needed.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. World Health Organization. BMI Classification. Available at: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html. Accessed on 22 February 2016.
2. Hartz AJ, Barboriak PN, Wong A, Katayama KP, Ri mm AA. The association of obesity with infertility and related menstrual abnormalities in women. Int J Obesity. 1979;3:57-73.
3. Talmor A, Dunphy B. Female obesity and infertility. Best Pract Res Clin Obstet Gynaecol. 2015;29:498-506.
4. Weiss JL, Malone FD, Emig D, Ball RH, Nyberg DA, Comstock CH et al. Obesity, obstetric complications, and cesarean delivery rate-a population-based screening study. Am J Obstet Gynecol. 2004;190:1091-7.
5. Brewer CJ, Balen AH. The adverse effect of obesity on conception and implantation. Reproduction J. 2010;140(3):347-64.
6. Valckx SD, de Pauw I, de Neubourg D, Inion I, Berth M, Fransen E et al. BMI-related metabolic composition of the follicular fluid of women undergoing assisted reproductive treatment and the consequences for oocyte and embryo quality. Hum Reprod. 2012;27:3531-9.
7. Rajasingam D, Seed PT, Briley AL, Shennan AH, Poston L. A prospective study of pregnancy outcome and biomarkers of oxidative stress in nulliparous obese women. Am J Obstet Gynecol. 2009;200:395.
8. Turner N, Robker RL. Developmental programming of obesity and insulin resistance: does mitochondrial dysfunction in oocytes play a role? Mol Hum Reprod. 2015;21(1):23-30.
9. Al-Mulhim AS, Al-Hussaini HA, Al-Jalal BA, Al-Moagal RO, Al-Najjar S. Obesity Disease and Surgery. Int J Chronic Dis. 2014;652341.
10. Luke B, Brown MB, Stern JE, Missmer SA, Fujimoto VY, Leach R. Female obesity adversely affects assisted reproductive technology (ART) pregnancy and live birth rates. Hum Reprod. 2011;26:245-52.
11. Bellver J, Mifsud A, Grau N, Privitera L, Meseguer M. Similar morphokinetic patterns in embryos derived from obese and normoweight infertile women: a time-lapse study. Hum Reprod. 2013;28(3):794-800.
12. Bellver J, Pellicer A, García-Velasco JA, Ballesteros A, Remohí J, Meseguer M. Obesity reduces uterine

receptivity: clinical experience from 9,587 first cycles of ovum donation with normal weight donors. Fertil Steril. 2013;100(4):1050-8.
13. Wang JX, Davies MJ, Norman RJ. Obesity increases the risk of spontaneous abortion during infertility treatment. Obes Res. 2002;10:551-4.
14. Dechaud H, Anahory T, Reyftmann L, Loup V, Hamamah S, Hedon B. Obesity does not adversely affect results in patients who are undergoing in vitro fertilization and embryo transfer. Eur J Obstet Gynecol Reprod Biol. 2006;127:88-9.
15. Kudesia R, Wu H, Hunter Cohn K, Tan L, Lee JA, Copperman AB, Yurttas BP. The effect of female body mass index on in vitro fertilization cycle outcomes: a multi-center analysis. J Assist Reprod Genet. 2018;35(11):201-23.
16. Zander-Fox DL, Henshaw R, Hamilton H, Lane M. Does obesity really matter? The impact of BMI on embryo quality and pregnancy outcomes after IVF in women aged ≤38 years. Aust N Z J Obstet Gynaecol. 2012;52(3):270-76.
17. Goldman KN, Hodes-Wertz B, McCulloh DH. Association of body mass index with embryonic aneuploidy. Fert sterility. 2015;103:744-8.
18. Meseguer M, Herrero J, Tejera A, Hilligsoe KM, Ramsing NB, Remoh J. The use of morphokinetics as a predictor of embryo implantation. Hum Reprod. 2011;26(10):2658-71.
19. Koning AM, Mutsaerts MA, Kuchenbecker WK, Broekmans FJ, Land JA, Mol BW et al. Complications and outcome of assisted reproduction technologies in overweight and obese women. Hum Reprod. 2012;27:457-67.
20. Bartolacci A, Buratini J, Moutier C, Guglielmo MC, Novara PV, Brambillasca F et al. Body mass index affects embryo morphokinetics: a time-lapse study. J Assist Reprod Genet. 2019;36(6):1109-16.
21. Metwally M, Ong KJ, Ledger WL, Li TC. Does high body mass index increase the risk of miscarriage after spontaneous and assisted conception? A meta-analysis of the evidence. Fertil Steril. 2008;90:714-26.
22. Shah DK, Missmer SA, Berry KF, Racowsky C, Ginsburg ES. Effect of obesity on oocyte and embryo quality in women undergoing *in vitro* fertilization. Obstet Gynecol. 2011;118:63-70.
23. Matalliotakis I, Cakmak H, Sakkas D, Mahutte N, Koumantakis G, Arici A. Impact of body mass index on IVF and ICSI outcome: a retrospective study. Reprod BioMed Online. 2008;16:778-824.
24. Stovezky YL, Romanski PA, Bortoletto P. Body mass index is not associated with embryo ploidy in patients undergoing in vitro fertilization with preimplantation genetic testing. Fertil Steril. 2021;116(2):388-95.
25. Sarais V, Pagliardini L, Rebonato G, Papaleo E, Candiani M, Viganò P. A Comprehensive Analysis of Body Mass Index Effect on in Vitro Fertilization Outcomes, nutrients J. 2016;8(3):109.
26. Einarsson S, Bergh C, Friberg B, Pinborg A, Klajnbard A, Karlström AO et al. Weight reduction intervention for obese infertile women prior to IVF: a randomized controlled trial. Human Reproduct. 2017;32(8):1621-30.

Cite this article as: Bahgat NA. Relation between maternal body mass index and embryo quality in normal responder young patients undergoing intracytoplasmic sperm injection cycle. Int J Reprod Contracept Obstet Gynecol 2022;11:2600-4.