Association between obesity and fecundity in patients undergoing intrauterine insemination

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Objective: To determine if an association exists between body mass index (BMI) and fecundity after intrauterine insemination (IUI).
Design: Retrospective cohort study.
Setting: Academic-based fertility clinic.
Patient(s): Patients undergoing IUI July 2007 to May 2012.
Intervention(s): None.
Main Outcome Measure(s): Primary outcome: live-birth rate (LBR) per IUI cycle; secondary outcomes: positive pregnancy test and clinical pregnancy rates (CPRs).
Result(s): A total of 1959 cycles were performed on 661 women (mean age, 31.9 ± 4.9 years). When examined by obesity class, LBR and CPR were similar for women with class I, II, and III obesity when compared with women with normal BMI. However, class III obese women (adjusted risk ratio [aRR], 1.70; 95% confidence interval [CI], 1.12–2.59) had increased pregnancy rates compared with normal BMI, but no differences in pregnancy rates were observed for women with class I or II obesity. In addition, pregnancy rates (aRR, 1.50; 95% CI, 1.12–2.02) and CPR (aRR, 1.51; 95% CI, 1.07–2.14) were higher in overweight women relative to normal BMI. Notably, among patients with ovulatory dysfunction, CPRs after IUI were reduced by 43% in obese women (aRR, 0.57; 95% CI, 0.37–1.07), whereas women without ovulatory dysfunction were twice as likely to achieve a clinical pregnancy when they were obese (aRR, 1.96; 95% CI, 1.19–3.24). The CIs for the obesity risk ratios in each stratum of ovulatory function exhibited no overlap, suggesting evidence of potential effect modification by ovulatory function.
Conclusion(s): LBRs after IUI were similar across BMI subgroups. This is in contrast to research of in vitro fertilization treatments showing lower LBR with increasing BMI. However, obesity may adversely affect IUI CPR in those with ovulatory dysfunction in particular. The reason for this discrepancy is unclear and warrants further study. (Fertil Steril Rep® 2023;4:270–8. ©2023 by American Society for Reproductive Medicine.)
Key Words: Intrauterine insemination, body mass index, obesity, fecundity, live birth

Obesity is a major public health issue that has been on the rise for decades. According to the Centers for Disease Control and Prevention, 42.4% of American adults aged >20 years are classified as obese on the basis of 2018 data, up from 30% in 2000, and those classified as severely obese has nearly doubled (4.7%–9.2%) in the same time frame (1). The World Health Organization uses body mass index (BMI; body weight in kilograms divided by height squared in meters) to define weight classes as follows: underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), obesity class I (30.0–34.9 kg/m^2), class II (35.0–39.9 kg/m^2), and class III (≥ 40.0 kg/m^2, also referred to as severe/morbidly obese by the Centers for Disease Control and Prevention) (2). It is well established that obesity can interfere with the ability of women to conceive (3–5). Moreover, those classified as overweight have been

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The subjects in this trial were not concomitantly involved in other randomized trials. Data regarding this same database were used for the following article: Craig LB, Arya S, Burks HR, Warta K, Jarshaw C, Hansen KR, et al. Relationship between semen regurgitation and pregnancy rates with intrauterine insemination. Fertil Steril 2021;116:1526–31. https://doi.org/10.1016/j.fertnstert.2021.07.1183. Epub 2021 Aug 18. Data will be made available to the editors of the journal for review or query on request.
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found to have menstrual cycle disturbances including protracted folliculogenesis, decreased luteal progesterone secretion (6), increased ovulatory dysfunction (7), altered ovarian responsiveness, and metabolic derangements including altered secretion and action of insulin (3, 4).

Obese women have a lower chance of conceiving in the general population and, therefore, a higher incidence of infertility at 1 year without contraception (4, 5, 8, 9). In fact, the risk of infertility is up to 3 times higher for those with a BMI of >30 kg/m^2 compared with women with a normal BMI (10). When patients with infertility undergo assisted reproductive technology treatments, such as in vitro fertilization (IVF), obesity is associated with lower pregnancy (11–13) and live-birth rates (LBRs) (11, 13–15) compared with women with a normal BMI. Relatively few studies have been published regarding the effect of obesity on pregnancy rates in less-aggressive and less-costly treatments, such as intrauterine insemination (IUI). The available studies have primarily focused on gonadotropins and IUI, showing either higher or no difference in pregnancy rates with obesity (16–18) in contrast to the IVF studies. In addition, studies investigating IUI have rarely evaluated ongoing pregnancy or LBRs (19, 20). Therefore, the objective of our study was to evaluate the impact of BMI on pregnancy and LBRs of patients undergoing IUI.

MATERIAL AND METHODS

This was a retrospective cohort study of all patients who underwent IUI between July 2007 and May 2012 at a university-affiliated infertility clinic. This included IUI procedures timed by ovulation predictor kits as well as those timed with ultrasound monitoring and human chorionic gonadotropin trigger shot. Cycles were excluded if 2 IUI procedures were performed in the same treatment cycle, 2 samples combined for IUI, lack of IUI procedure documentation, retrograde ejaculation, partner reported sample spill during collection or transportation of the sample, pregnancy outcome unknown, and/or missing covariate data including BMI. Cycles canceled before IUIs were not captured in the database. Demographic information was obtained including the woman's age, ethnicity, BMI, total motile count (calculated as volume [mL] × count [million/mL] × % motility) of sperm inseminated, duration of infertility, concurrent fertility medication(s), and infertility diagnoses. The primary outcome was live birth at ≥24 weeks gestation. The secondary outcomes were positive pregnancy test per cycle defined as a serum quantitative hCG > 10 mIU/mL 15 days after IUI and clinical pregnancy rate defined as an intrauterine gestation with fetal heartbeat in the first trimester by transvaginal ultrasound. Delivery outcomes of 74 clinical pregnancies were unconfirmed and excluded from analyses of live births but were included in the secondary outcome analyses, which represents a sensitivity analysis for best case scenario where all unconfirmed deliveries are assumed to result in live births. These unconfirmed deliveries had 2 first trimester transvaginal ultrasounds confirming good interval growth before beginning obstetrical care. They were then lost to follow-up. The study was reviewed and approved by the Institutional Review Board at the University of Oklahoma Health Sciences Center (IRB#2084).

Patient characteristics recorded at the first clinic visit during the study period were compared with BMI using chi-square tests or Fisher exact tests for categorical variables.

Data from all patient cycles were used to evaluate the association between BMI and IUI treatment outcome. We fit modified Poisson regression models with robust standard errors including a log link function and independent working correlation structure to estimate risk ratios (RRs) and 95% confidence intervals (95% CIs). Informative clustering may occur when the number of IUI cycles per couple is influenced by previous treatment outcomes. Therefore, to address this concern, the cluster-weighted model was fit by weighting the generalized estimating equations score equation by the inverse of the number of IUI cycles completed for each couple (10, 11). Adjusted models (adjusted RR [aRR]; variables decided a priori) were controlled for women's age (<34, 35–39, ≥40 years), race/ethnicity (non-Hispanic white, Hispanic, Black, Asian, and American Indian), BMI (<18.5, 18.5–24.9, 25–29.9, 30.0–34.99, 30–35, ≥40 kg/m^2), duration of infertility (<3, ≥3years), infertility diagnoses (ovulatory, tubal, endometriosis, male factor, unexplained, other), medication used for ovulation induction or ovarian stimulation (none, clomiphene citrate, letrozole, gonadotropins), total motile sperm count (≤5, >5–10, >10–20, >20–30, >30 million), and sperm source (partner or donor sperm). Stratification by treatment was of interest because of higher fecundity in IUI cycles with gonadotropins; however, the small number of gonadotropin cycles did not support stratified analysis. Therefore, analyses were repeated after excluding patients treated with gonadotropins, knowing pregnancy rates are higher than the other treatments. In addition, unadjusted and adjusted models were evaluated in strata defined by the presence or absence of ovulatory dysfunction. The stratified analyses collapsed all BMI categories that were ≥30 into a single obesity category to account for smaller cell sizes that resulted from stratification. Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC).

RESULTS

A total of 2221 IUI cycles were completed in the study timeframe on 719 women. A total of 262 cycles were excluded: 8 had 2 IUIs performed in the same treatment cycle; 17 had 2 samples combined for IUI, 6 had incomplete documentation of IUI procedure, 8 had retrograde ejaculation, 12 cycles the partner reported sample spill during collection or transportation of the sample, 63 cycles the IUI outcome completely unknown, and 148 cycles had missing covariate data including 9 with missing BMI. Therefore, results are reported for 1959 IUI cycles in 661 women. The patient and cycle characteristics by BMI are shown in Table 1. Pregnancy rates overall were 15.3% per IUI cycle with the mean age of women as 31.9 ± 4.9 years.

The associations between BMI and outcomes of positive pregnancy test, clinical pregnancy, and live birth are shown in Table 2. Pregnancy rates were higher for those in the

TABLE 1

Distribution of characteristics of 661 patients undergoing intrauterine insemination by body mass index (BMI).

BMI (kg/m^2)

Patient characteristics at baseline	< 18.5 (n = 16) n (%)	18.5 to < 25 (n = 267) n (%)	25 to < 30 (n = 169) n (%)	30 to < 35 (n = 89) n (%)	35 to < 40 (n = 56) n (%)	≥40 (n = 64) n (%)	P[a]
Race/ethnicity[b]							
Non-Hispanic White	13 (81.3)	218 (81.7)	128 (75.7)	73 (82.0)	44 (78.6)	50 (78.1)	.0009[c]
Black	0 (0.0)	4 (1.5)	10 (5.9)	6 (6.7)	1 (1.8)	5 (7.8)	
American Indian	0 (0.0)	7 (2.6)	6 (3.6)	5 (5.6)	6 (10.7)	6 (9.4)	
Hispanic	2 (12.5)	14 (5.2)	11 (6.5)	0 (0.0)	4 (7.1)	3 (4.7)	
Asian	1 (6.3)	24 (9.0)	14 (8.3)	5 (5.6)	1 (1.8)	0 (0.0)	
Age, y							.77
<34	13 (81.3)	193 (72.3)	122 (72.2)	64 (71.9)	35 (62.5)	44 (68.8)	
35–39	2 (12.5)	49 (18.4)	33 (19.5)	19 (21.4)	17 (30.4)	16 (25.0)	
≥40	1 (6.3)	25 (9.4)	14 (8.3)	6 (6.7)	4 (7.1)	4 (6.3)	
Years of infertility, y							
≥3	6 (37.5)	100 (37.5)	63 (37.3)	42 (47.2)	24 (42.9)	31 (48.4)	.38
<3	10 (62.5)	167 (62.6)	106 (62.7)	47 (52.8)	32 (57.1)	33 (51.6)	
Total motile sperm count[b]							
≤5	2 (12.5)	51 (19.1)	29 (17.2)	15 (16.9)	13 (23.2)	10 (16.5)	.32
>5–10	2 (12.5)	52 (19.5)	30 (17.8)	25 (28.1)	11 (19.6)	14 (21.9)	
>10–20	4 (25.0)	67 (25.1)	51 (30.2)	26 (29.2)	19 (33.9)	20 (31.3)	
>20–30	6 (37.5)	34 (12.7)	24 (14.2)	8 (9.0)	8 (14.3)	9 (14.1)	
>30	2 (12.5)	63 (23.6)	35 (20.7)	15 (16.9)	5 (8.9)	11 (17.2)	
Endometriosis							.04
Yes	3 (18.8)	40 (15.0)	13 (7.7)	11 (12.4)	5 (8.9)	2 (3.1)	
No	13 (81.3)	227 (85.0)	156 (92.3)	78 (87.6)	51 (91.1)	62 (96.9)	
Ovulatory diagnosis							
Yes	5 (31.3)	65 (24.3)	56 (33.1)	43 (48.3)	28 (50.0)	40 (62.5)	< .0001
No	11 (68.8)	202 (75.7)	113 (66.7)	46 (51.7)	28 (50.0)	24 (37.5)	
Tubal diagnosis[c]							
Yes	1 (6.3)	11 (4.1)	11 (6.5)	3 (3.4)	2 (3.6)	3 (4.7)	.80[c]
No	15 (93.8)	256 (95.9)	158 (93.5)	86 (96.6)	54 (96.4)	61 (95.3)	
Unexplained diagnosis							
Yes	3 (18.8)	73 (27.3)	45 (26.6)	6 (6.7)	2 (3.6)	7 (10.9)	< .0001
No	13 (81.3)	194 (72.7)	124 (73.4)	83 (93.3)	54 (96.4)	57 (89.1)	
Other diagnosis							
Yes	2 (12.5)	26 (9.7)	20 (11.8)	16 (18.0)	7 (12.5)	4 (6.3)	.27
No	14 (87.5)	241 (90.3)	149 (88.2)	73 (82.0)	49 (87.5)	60 (93.8)	
Sperm source							.003
Partner	16 (100.0)	248 (92.9)	156 (92.3)	78 (87.6)	43 (76.8)	55 (85.9)	
Donor	0 (0.0)	19 (7.1)	13 (7.7)	11 (12.4)	13 (23.2)	9 (14.1)	
Cycle characteristics	**n = 43**	**n = 792**	**n = 495**	**n = 290**	**n = 166**	**n = 173**	
Ovulation monitoring							d
Ultrasound/trigger shot	31 (72.1)	681 (86.0)	423 (85.5)	254 (87.6)	153 (92.2)	152 (87.9)	
Ovulation predictor kit	12 (27.9)	111 (14.0)	72 (14.6)	36 (12.4)	13 (7.8)	21 (12.1)	

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TABLE 1

Continued.

Cycle characteristics	n = 43	n = 792	n = 495	n = 290	n = 166	n = 173	
Medications[b]							d
None (natural)	0 (0.0)	48 (6.1)	16 (3.2)	17 (5.9)	7 (4.2)	8 (4.6)	
clomiphene citrate	35 (81.4)	565 (71.3)	359 (72.5)	211 (72.8)	101 (60.8)	125 (72.3)	
Letrozole	3 (7.0)	103 (13.0)	81 (16.4)	25 (8.6)	36 (21.7)	17 (9.8)	
Gonadotropins	5 (11.6)	76 (9.6)	38 (7.7)	37 (12.8)	22 (13.3)	23 (13.3)	

[a] Chi-square test
[b] Total motile sperm count is volume (mL) × count (million/mL) × % motility.
[c] Monte Carlo estimate of Fisher exact test.
[d] Chi-square tests are not estimated for cycle characteristics because of lack of independent observations.

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overweight (aRR, 1.50; 95% CI, 1.12–2.02) and the morbidly obese BMI category (aRR, 1.70; 95% CI, 1.12–2.59) compared with those in the normal BMI range. The pregnancy rate per cycle was similar for subjects with class I or II obesity when compared with women with a normal BMI; however, clinical pregnancy rates (CPRs) were increased only in the overweight group. Similar to the estimates observed for positive pregnancy tests, estimates for live births were modestly increased for overweight and class III women compared with normal BMI, but the CIs were imprecise and crossed 1.0. When class I, class II, and class III obesity groups were combined into a single category (BMI $\geq$ 30 kg/m^2) representing obesity, pregnancy rates in women with obesity were modestly higher compared with women with normal BMI (aRR, 1.38; 95% CI, 1.00–1.93) but clinical pregnancy (aRR, 1.15; 95% CI, 0.74–1.77) and LBRs (aRR, 1.07; 95% CI, 0.60–1.90) were similar, with point estimates near 1.0. Across all outcomes evaluated, the estimated RRs for underweight women were consistently <1.0, which suggested lower rates of pregnancy, clinical pregnancy, and live birth, but these estimates were on the basis of few events and the CIs were wide, which indicated a greater degree of uncertainty. Subanalyses for pregnancy loss demonstrated a strong pattern of increasing loss with obesity, but the data were limited because of incomplete ascertainment of outcomes for the 74 unconfirmed deliveries/ongoing pregnancies (data not shown).

Knowing that IUI cycles with gonadotropins have higher cycle fecundity and that the majority of our patients took clomiphene citrate or letrozole, the analysis was repeated in 617 patients undergoing 1758 IUI cycles excluding the gonadotropin cycles. In this restricted subset, the results remained essentially unchanged for all outcomes (Supplemental Table 1).

When stratified by ovulatory function, the obesity RRs for women with and without ovulatory function were in opposing directions for all outcomes (Table 3). In women without ovulatory dysfunction, pregnancy tests, clinical pregnancy, and live births were increased in obese women compared with normal BMI, although the CI for live birth included values <1.0. In those with ovulatory dysfunction, all RRs for obesity were <1.0 with CIs spanning the null value. Notably, among women with ovulatory dysfunction, CPRs after IUI were reduced by 43% in obese women (aRR, 0.57; 95% CI, 0.31–1.07), whereas women without ovulatory dysfunction were twice as likely to achieve a clinical pregnancy when they were obese (aRR, 1.96; 95% CI, 1.19–3.24). The CIs for the obesity RRs for pregnancy tests and clinical pregnancy in each stratum of ovulatory function exhibited little or no overlap, suggesting evidence of potential effect modification by ovulatory function.

DISCUSSION

The major finding of our study indicates that there is no difference in LBRs among ovulatory patients with a normal or elevated BMI undergoing IUI. Moreover, a positive association exists between increased BMI and pregnancy rates among certain BMI classes (overweight and class III obesity). The handful of studies available assessing the impact of

TABLE 2

Associations between body mass index (BMI) and outcomes of positive pregnancy test, clinical pregnancy, and live birth among 661 patients undergoing 1959 intrauterine insemination cycles

	Cycles n	Outcomes n (%)	Unadjusted RR[b] (95% CI)	Adjusted RR[b,c] (95% CI)
Positive pregnancy test				
BMI				
<18.5	43	4 (9.3)	0.75 (0.26–2.17)	0.74 (0.27–2.04)
18.5 to <25	792	105 (13.3)	1.00 (Referent)	1.00 (Referent)
25 to <30	495	88 (17.8)	1.49 (1.11–2.02)	1.50 (1.12–2.02)
30 to <35	290	42 (14.5)	1.21 (0.82–1.77)	1.33 (0.89–1.99)
35 to <40	166	23 (13.9)	0.95 (0.57–1.57)	1.10 (0.65–1.87)
≥40	173	37 (21.4)	1.56 (1.05–2.30)	1.70 (1.12–2.59)
Clinical pregnancy				
BMI				
<18.5	43	3 (7.0)	0.76 (0.22–2.67)	0.76 (0.23–2.54)
18.5 to <25	792	77 (9.7)	1.00 (Referent)	1.00 (Referent)
25 to <30	495	64 (12.9)	1.50 (1.06–2.13)	1.51 (1.07–2.14)
30 to <35	290	26 (9.0)	1.10 (0.68–1.77)	1.20 (0.72–2.00)
35 to <40	166	14 (8.4)	0.83 (0.43–1.58)	0.99 (0.50–1.96)
≥40	173	16 (9.3)	1.05 (0.59–1.85)	1.18 (0.63–2.20)
Live birth[a]				
BMI				
<18.5	41	1 (2.4)	0.76 (0.11–5.17)	0.83 (0.14–4.89)
18.5 to <25	765	50 (6.5)	1.00 (Referent)	1.00 (Referent)
25 to <30	467	36 (7.7)	1.36 (0.83–2.24)	1.34 (0.84–2.14)
30 to <35	280	16 (5.7)	0.83 (0.43–1.62)	0.89 (0.43–1.84)
35 to <40	162	10 (6.2)	0.81 (0.37–1.79)	0.94 (0.42–2.12)
≥40	170	13 (7.7)	1.32 (0.67–2.57)	1.41 (0.66–3.05)

[a] Models examining live birth outcomes include 1885 cycles among 587 patients after excluding 74 ongoing clinical pregnancies with unconfirmed outcomes.
[b] Risk ratios (RR) and 95% confidence intervals (95% CIs) were calculated using a cluster-weighted generalized estimating equation method to estimate modified Poisson regression models with robust standard errors.
[c] Adjusted risk ratios were adjusted for age, race/ethnicity, total motile sperm count, infertility duration, infertility diagnosis, sperm source, method of intrauterine insemination timing, and medications.

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obesity on pregnancy outcomes during IUI cycles have been inconsistent and mainly focus on ovarian stimulation with gonadotropins (16–19, 21). With similar results to our study, Wang et al. (21) observed an increase in pregnancy rates for overweight (30% more) and obese patients (50% more) undergoing IUI compared with those of a normal BMI, but the subjects in this study only used gonadotropins and not clomiphene citrate or letrozole, which is a trend supported by 2 similar studies (16, 19). In one of the few studies that followed pregnancy through to delivery, Souter et al. (19) found that overweight and obese BMI groups had overall higher odds of achieving pregnancy than their healthy and underweight counterparts with the use of gonadotropins; however, only the overweight BMI group displayed higher odds of live birth (overweight: aRR, 1.91; 95% CI, 1.2–3.2; obese: aRR, 1.8; 95% CI, 0.96–3.5). In contrast, Wolff et al. reported no evidence of association between obesity and the cycle-related fecundity in patients undergoing ovarian stimulation with gonadotropins and IUI (18).

Three studies have described a negative correlation between BMI and pregnancy rates in patients undergoing ovarian stimulation with gonadotropins and IUI procedures (22–24). Apart from their use of gonadotropins, each of these studies utilized nonstandard BMI ranges and cutoffs, which make comparison with our study difficulty. Koloszar et al. (22) found that women with a BMI of 28–36 kg/m^2 had half the success (21% pregnancy/cycle) compared with women with a BMI of 20–24 kg/m^2 (42% pregnancy/cycle). A BMI of >36 kg/m^2 is progressively more common in the United States, and studies that exclude this subset of patients offer limited generalizability. Yavus et al. (23) had an overall pregnancy rate of only 4.7%, which is significantly lower than the average success rate of this procedure. In addition, Na et al. (24) did not separate ovulatory patients from those with ovulatory dysfunction.

We could only identify 2 studies in the literature that investigated the impact of BMI on pregnancy rates with the use of letrozole during IUI. McKight et al. (17) determined that women in BMI ranges of ≥30 kg/m^2 had higher pregnancy outcomes compared with women with a BMI of <30 when undergoing IUI treatment with letrozole, although this result was not statistically significant (per unit BMI increase: RR, 1.093; 95% CI, 1.008–1.184; P=.14). Utilizing data from the Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation clinical trial including 900 couples with unexplained infertility, Hansen et al (25) did not identify a relationship between live birth, BMI, or waist-to-hip ratio (WHR). A recent study from 2021 evaluating IUI outcomes to delivery with a treatment arm of clomiphene citrate/letrozole found that BMI did not have a negative effect on pregnancy rate, delivery, or live birth (20). In contrast to our study, Whynott et al. (20) determined

TABLE 3

Associations between body mass index (BMI) and outcomes of positive pregnancy test, clinical pregnancy, and live birth among patients with and without ovulatory dysfunction undergoing intrauterine insemination cycles

	With ovulatory dysfunction (684 cycles among 237 patients)[a]			Without ovulatory dysfunction (1270 cycles among 424 patients)		
	Outcomes/total (%)	Unadjusted RR[b] (95% CI)	Adjusted RR[b,c] (95% CI)	Outcomes/total (%)	Unadjusted RR[b] (95% CI)	Adjusted RR[b,c] (95% CI)
Positive pregnancy test						
BMI						
<18.5	1/11 (9.1%)	0.91 (0.15–5.41)	1.04 (0.20–5.42)	3/32 (9.4%)	0.61 (0.21–1.81)	0.59 (0.21–1.66)
18.5 to <25	31/190 (16.3%)	1.00 (Referent)	1.00 (Referent)	74/599 (12.4%)	1.00 (Referent)	1.00 (Referent)
25 to <30	32/153 (20.9%)	1.50 (0.92–2.43)	1.50 (0.92–2.47)	56/342 (16.4%)	1.42 (0.98–2.07)	1.46 (1.01–2.13)
≥30	57/330 (17.3%)	0.86 (0.55–1.35)	0.86 (0.53–1.39)	45/297 (15.2%)	1.58 (1.06–2.35)	1.98 (1.32–2.95)
Clinical pregnancy						
BMI						
<18.5	1/11 (9.1%)	1.0 5(0.17–6.37)	1.17 (0.22–6.17)	2/32 (6.3%)	0.51 (0.12–2.16)	0.52 (0.12–2.26)
18.5 to <25	24/190 (12.6%)	1.00 (Referent)	1.00 (Referent)	53/599 (8.9%)	1.00 (Referent)	1.00 (Referent)
25 to <30	24/153 (15.7%)	1.52 (0.87–2.65)	1.52 (0.86–2.67)	40/342 (11.7%)	1.40 (0.90–2.19)	1.47 (0.95–2.28)
≥30	26/330 (7.9%)	0.55 (0.30–1.00)	0.57 (0.31–1.07)	30/297 (10.1%)	1.51 (0.94–2.44)	1.96 (1.19–3.24)
Live birth[d]						
BMI						
<18.5	1/11 (9.1%)	1.90 (0.30–12.14)	2.23 (0.43–11.53)	0/30 (0.0%)[e]	–	–
18.5 to <25	14/180 (7.8%)	1.00 (Referent)	1.00 (Referent)	36/582 (6.2%)	1.00 (Referent)	1.00 (Referent)
25 to <30	15/144 (15/10.4%)	1.54 (0.67–3.56)	1.57 (0.68–3.63)	21/323 (6.5%)	1.23 (0.66–2.28)	1.23 (0.68–2.20)
≥30	19/323 (5.9%)	0.71 (0.32–1.57)	0.73 (0.32–1.69)	20/287 (7.0%)	1.25 (0.66–2.35)	1.47 (0.72–3.01)

[a] Stratum with ovulatory dysfunction excludes 5 natural cycles to address model convergence problems because of sparse data in this group.
[b] Risk ratios (RR) and 95% confidence intervals (95% CIs) were calculated as cluster-weighted generalized estimating equation method to estimate modified Poisson regression models with robust standard errors.
[c] Adjusted models controlled for age, race/ethnicity, total motile sperm count, infertility duration, infertility diagnosis, sperm source, method of IUI timing, and medications.
[d] Models examining live-birth outcomes excluded ongoing clinical pregnancies with unconfirmed outcomes. The stratum with ovulatory dysfunction included 663 cycles among 211 patients. The stratum without ovulatory dysfunction included 1192 cycles among 367 patients.
[e] Analysis excludes BMI <18.5 to address model convergence problems because of no events in this group.

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that anovulation was positively correlated with live birth (aRR, 1.97; 95% CI, 1.45–2.69; $P<.001$). However, when they subclassified by obesity classes, LBRs no longer differed from normal BMI class. Finally, although various studies have found a positive association with BMI and pregnancy rates but no association with BMI and live birth, none of these studies have found a relationship between BMI and miscarriage when powered to do so (25, 20). Understanding any impact of BMI on the outcome of live birth is relevant to enable holistic preprocedural counseling.

In contrast to IUI and obesity, there are numerous studies evaluating the effects of BMI and pregnancy rates in IVF and other assisted reproductive technology treatments (11–14, 26, 27). These studies have described lower pregnancy and LBRs with an obese BMI classification (11, 13, 14). Petersen et al. (14) found that the chance of live birth was decreased in IVF by 2% for every 1 unit increase in BMI. Luke et al. (11) additionally detail a decrease in fecundity, length of gestation, and LBR as BMI increased in patients undergoing IVF, compounded by increasing age and BMI. Although a few studies have not found an association between high BMI and IVF success (26, 27), these appear to be outliers as confirmed by a recent meta-analysis on this subject (12).

Several theories have been proposed to explain the differing results between BMI and the success rates of IUI and IVF. The primary reason, suggested by several studies, is the obstacle of subtle abnormalities of ovulation with relation to obesity (4, 5, 21, 28, 29), which is managed in IUI treatments combined with ovarian stimulation. Consistent with this assertion, our study provides evidence of effect modification of the obesity and IUI outcome association by ovulatory function. Among patients with outright ovulatory dysfunction, CPRs were reduced when comparing obese women with those with normal BMI. In contrast, a positive relationship was observed between obesity and clinical pregnancy in ovulatory patients. Therefore, subtle hormonal imbalances are corrected with ovarian stimulation and IUI, and not just outright anovulation with increasing obesity. Another theory involves obesity's effects on uterine receptivity, including impact on endometrial thickness (EMT). Although a few studies investigating IUI have found a positive association between BMI, EMT, and pregnancy rates (18, 19), a majority have displayed mixed results and all agree that EMT is a poor single predictor of pregnancy outcomes (30, 31). Studies reporting a negative correlation between WHR and pregnancy/live birth after IUI—one even describing a 0.1 unit increase leads to a 30% decrease in pregnancy—further highlight the hormonal irregularities associated with central obesity and that fat mass index or body fat mass are typically more predictive (32–34). Although the large multicenter Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation study did not find a relationship between insulin resistance, pregnancy rate, or LBRs (25), WHR may be a better measure of obesity than BMI in understanding the likelihood of success with IUI. A final theory is that good prognosis obese patients are able to achieve pregnancy with less-aggressive treatments, leaving the poorer prognosis obese patients to undergo IVF with resultant lower pregnancy rates. It is clear that the difference in outcomes in obese patients between IUI and IVF is likely multifactorial.

Even if a high BMI does not adversely impact the pregnancy rates after IUI, we must continue to consider the impact of maternal obesity on the patient's health and the health of the infant. Several studies have found the risk of cesarean delivery and resultant wound infections, early birth, and miscarriage increase with BMI (15, 24, 33, 35–37). Studies have found a negative relationship between maternal BMI and the birthweight of offspring, as well as increased likelihood of NICU stay, developmental delays, and onset of comorbidities early in childhood (35, 37, 38). It is almost impossible to truly distinguish between the various elements, such as poor nutrition or uptake of available nutrition in utero, and other confounding factors, such as socioeconomic status and access to healthcare (39). A large meta-analysis by D'Souza et al. (36) found a linear relationship between maternal BMI and all adverse pregnancy outcomes for both mother and infant. Awareness of these risks is critical to optimize counseling before infertility treatment and throughout pregnancy.

The strengths of our study include the large number of IUI cycles included and the adjustment for multiple confounding factors as well as informative clustering among multiple cycles per patient. Our study is one of a few to evaluate the impact of BMI on LBRs in IUI cycles and not just pregnancy rates. We were able to control for clomiphene citrate, letrozole, and gonadotropins in the analysis. However, the numbers in the gonadotropin and letrozole group were too small to report outcomes separately. Our study would have been improved with evaluation of WHR or body fat mass, both of which could provide a better measure of obesity and metabolic disturbance than BMI (25, 32–34). The US population with class III obesity has nearly doubled since the data were collected for this study (2), and therefore, deserves ongoing evaluation. Only one geographic center was included in this study; therefore, the generalizability of the findings is limited to practices with similar patient characteristics. In addition, we did not capture adjunct medications, such as luteal progesterone of metformin. Furthermore, the cycles that were canceled before IUI were not included in the database, and therefore, we cannot assess the impact of BMI on cycle cancelation. The exclusion of unconfirmed deliveries from analyses of live birth could introduce a selection bias if confirmation differed by the patient's BMI and delivery outcome. In addition, we were unable to obtain information on maternal and fetal complications of pregnancy, which have been well evaluated in IVF (12), but in only one study evaluating IUI cycles (24).

Obesity is a major epidemic that is unlikely to improve any time soon. Our study confirms findings of others that in less-aggressive treatments, higher BMI do not lower pregnancy or LBRs in patients without ovulatory dysfunction. Although the health of the potential child and general success

and complications of pregnancy must remain an important component of preconception counseling, fertility specialists should be conscious of implicit bias toward obese patients to ensure that it does not impede the delivery of evidence-based clinical care (40). Future studies should include WHR and body fat mass to better measure body fat distribution and obesity, which could potentially be a better indicator of fertility trends (25, 32–34). Future studies on BMI affecting pregnancy outcomes in IUI cycles should follow patients after delivery to evaluate if the maternal and fetal complications are the same as those found in IVF cycles. Above all else, more studies of the effects of BMI on pregnancy outcome in IUI cycles are needed to properly inform patients of the true risks of IUI treatment and allow patients to make informed decisions for themselves and their family.

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