Obesity is associated with an increased risk of early pregnancy loss after euploid frozen embryo transfer

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Objective: To determine whether obesity is associated with an increased risk of pregnancy loss in patients undergoing autologous euploid frozen embryo transfer (FET).
Design: Retrospective cohort study.
Subjects: Patients with recorded body mass index (BMI) from nine clinical sites during January 2019 to December 2024, undergoing their first, autologous, single, euploid FET were included. Other preimplantation genetic testing indications were excluded.
Exposure: Patients were stratified into two groups: patients with obesity (BMI $\geq$30.0 kg/m^2) and nonobese patients (BMI $<$30.0 kg/m^2).
Main Outcome Measures: Primary outcome was biochemical pregnancy loss (beta human chorionic gonadotropin [β-hCG] $>$5 mIU/mL without ultrasound evidence of pregnancy until β-hCG $<$5 mIU/mL) or clinical pregnancy loss (ultrasound evidence of at least an intrauterine gestational sac, which did not progress to live birth). Secondary outcomes included implantation, ectopic, clinical and ongoing pregnancy (8–9 weeks gestational age with cardiac activity), and live birth (neonate $>$24 weeks gestational age).
Results: A total of 14,990 patients were included: 11,179 nonobese and 3,811 with obesity. Compared with nonobese, patients with obesity were older. Parity, antimüllerian hormone (AMH) levels, and blastulation day were similar between groups. After adjustment, patients with obesity had a 19% increased risk of pregnancy loss (adjusted relative risk [aRR]: 1.19, 95% confidence interval [CI] 1.14–1.24) compared with nonobese. When stratified by BMI categories, class I (BMI 30.0–34.9 kg/m^2), II (BMI 35.0–39.9 kg/m^2), and III (BMI $\geq$40.0 kg/m^2) obesities had 13%, 20%, and 42% increased risk of pregnancy loss, respectively, whereas the underweight (BMI $<$18.0 kg/m^2) and overweight (BMI 25.0–29.9 kg/m^2) groups performed similarly to the normal-weight group (BMI 18.5–24.9 kg/m^2). The predicted probability of pregnancy loss was lowest at a BMI of 25.3 kg/m^2. Although there was no difference in implantation (aRR: 0.98, 95% CI 0.86–1.37), patients with obesity had lower chances of clinical (aRR: 0.96, 95% CI 0.94–0.99) and ongoing pregnancy (aRR: 0.94, 95% CI 0.92–0.96) and live birth (aRR: 0.92, 95% CI 0.91–0.94). Risk of pregnancy loss was attenuated in parous patients with obesity (aRR: 0.90, 95% CI 0.79–1.02).
Conclusion: When accounting for embryonic aneuploidy in the setting of euploid-only transfers, patients with obesity had a 19% increased risk of early pregnancy loss compared with nonobese patients, with risk rising across BMIs and BMI categories. (Fertil Steril® 2026;126:265–74. ©2026 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Obesity, body mass index, frozen embryo transfer, euploid blastocysts, pregnancy loss

The National Center for Health Statistics, from August 2021 to August 2023, reported that the prevalence of obesity, defined as a body mass index (BMI) $>$30 kg/m^2, was 41.3%, and the prevalence of severe obesity (BMI $\geq$40 kg/m^2) was 12.1% among women in the United States (1). In 2023, the March of Dimes, a US nonprofit organization focused on maternal health, reported 33.5% of reproductive-aged women as obese; an 8.4% increase since 2012 (2). Although obesity and infertility are distinct entities, it is well established that obesity adversely impacts reproductive function through several mechanisms, including disruption of ovulatory processes and impairment of oocyte and follicular development,

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significantly decreasing conception and fecundity (3, 4). Given the increasing prevalence of obesity, paired with other societal factors delaying parenthood, more women with obesity are seeking assisted reproductive technologies (ART) to achieve pregnancy. This shift is highlighted in studies using the Society for Assisted Reproductive Technology Clinic Outcome Reporting Systems (2014–2019), where 24%–34% of in vitro fertilization (IVF) patients were overweight (BMI $\geq$25.0–29.9 kg/m^2) and 17.2%–20.7% were obese (5, 6).

Although obesity and reproduction are linked, the effects on ART outcomes are not well established. Obesity may impact ovarian response to stimulation and influence oocyte quality, whereas hormonal imbalances and inflammation may alter endometrial function (3). Bellver et al. (7) analyzed over 30,000 patients and embryo transfers, finding women with obesity less reproductively efficient. They concluded that women with obesity required a greater number of oocytes, embryos, and transfers to achieve live birth rates similar to those of normal-weight women (7). This evidence suggests a more arduous reproductive journey for women with obesity. However, Kim et al. (8) found no differences in embryologic or pregnancy outcomes among patients undergoing IVF on the basis of BMI in a prospective cohort study, suggesting the literature remains conflicted.

Much of the data on obesity and IVF outcomes stems from oocyte donors and obese egg recipients, which control for oocyte quality and isolate the effects of obesity on the uterus (9–13). However, the ideal scenario for most IVF patients is having biological offspring. Furthermore, prior studies have predominantly focused on the outcome of live birth, without analyzing potential adverse IVF outcomes associated with obesity (6, 13–17). Indeed, there are limited data regarding the role of obesity in IVF pregnancy loss, which can lead to significant emotional anguish and influence the likelihood of treatment abandonment (18). Moreover, prior studies have not included entire cohorts using preimplantation genetic testing for aneuploidy (PGT-A), which reduces embryonic aneuploidy, the most common etiology of pregnancy loss (19–21).

This study aimed to determine whether obesity is associated with an increased risk of pregnancy loss following autologous, euploid, frozen single-blastocyst embryo transfer. By limiting transfers to PGT-A euploid embryos, losses attributable to embryonic aneuploidy were minimized, allowing a focused evaluation of nonaneuploid contributors to pregnancy loss. The exclusive use of frozen embryo transfer (FET) further standardized implantation conditions by optimizing embryo-endometrial synchrony. Together, these design elements helped isolate the effect of maternal obesity on pregnancy loss. Given the rising prevalence of both obesity and infertility, clarifying this relationship is essential to improve individualized patient counseling, expectation setting, and treatment planning.

MATERIALS AND METHODS

Inclusion and exclusion criteria

This was a retrospective cohort study conducted at an infertility network (Reproductive Medicine Associates), including nine sites (New Jersey, Philadelphia, Florida, Northern and Southern California, Colorado, Seattle, Houston, and San Diego) between January 2019 and December 2024. Patients undergoing first, autologous, FET using a single blastocyst negative for whole chromosome aneuploidy via a single PGT-A assay with a recorded BMI and known transfer outcome were included (19). Patients with recurrent pregnancy loss (RPL) and transfers involving preimplantation genetic testing for monogenic disorders (PGT-M) or preimplantation genetic testing for structural rearrangements (PGT-SR), segmental or mosaic findings, untested or no result embryos, >1 biopsy or thaw procedure and ancillary PGT assays were excluded. Institutional review board (IRB) approval was obtained via an exemption determination for retrospective research (Advarra IRB Pro00064197).

Data collection

Height (inches) and weight (lbs) obtained at a clinic visit approximately 1 year before FET, recorded BMI, demographic variables, and outcomes were extracted from the electronic medical record (EMR). When more than one infertility diagnosis was present, the primary diagnosis was used. Uterine factor infertility included the following diagnoses: uterine fibroids (intramural, submucosal, or unspecified), endometrial polyps, adenomyosis, uterine septum, and intrauterine adhesions. All patients with uterine pathology underwent routine evaluation and management, followed by confirmation of a normal uterine cavity before transfer. All data were reviewed and validated for accuracy and completeness.

Ovarian stimulation protocols

Routine ovarian stimulation, trigger for oocyte maturation and retrieval procedures were performed, including intracytoplasmic sperm injection, day 3 assisted hatching, extended culture and vitrification at the blastocyst stage with trophectoderm biopsy performed on day 5, 6, or 7 according to standard embryology protocols. PGT-A was performed on a single, validated platform (19).

Frozen embryo transfer endometrial preparation protocols

Standard FET protocols, including programmed (exogenous estrogen and progesterone [P4]), modified natural (modified natural cycle [mNC] with human chorionic gonadotropin [hCG] trigger), or stimulated (gonadotropins or letrozole), were selected by the provider on the basis of patient characteristics or preference. All cycles included baseline transvaginal ultrasound and serum hormone assessments (estradiol [E2], P4, beta hCG and, if applicable, luteinizing hormone [LH]) on cycle days 2–4. Programmed cycles used oral Estrace (2 mg, 2–3 times daily) with monitoring until endometrial thickness reached $\geq$7 mm when intramuscular progesterone in oil was initiated (50 mg daily). In mNCs, follicular monitoring began around cycle day 10, with hCG trigger administered when a dominant follicle (approximately 18 mm mean sac diameter) or LH surge was present, followed by

vaginal prometrium (200 mg twice daily). Stimulated cycles were monitored until a dominant follicle developed after which an hCG trigger was administered and vaginal prometrium was started. All FET procedures occurred on the 6th day of progesterone exposure.

Exposure

Patients were stratified into two groups: the obese group, defined as a BMI $\geq$30.0 kg/m^2 and the nonobese group, defined as a BMI $\leq$29.9 kg/m^2.

Outcomes

The primary outcome was pregnancy loss (biochemical: serum β-hCG >5 mIU/mL without ultrasound evidence of pregnancy; or clinical: ultrasound evidence of an intrauterine gestational sac that did not progress to live birth and was neither terminated nor ectopic). Secondary outcomes included implantation (serum β-hCG >5 mIU/mL), clinical, ectopic, and ongoing pregnancy (8–9 weeks' gestational age with cardiac activity) as well as live birth (>24 weeks' gestational age).

Statistical analyses

Descriptive statistics using measures of central tendency and dispersion were calculated to describe baseline characteristics. Wilcoxon's rank sum test, Student's *t*-test, and Pearson's χ^2 were used for continuous and categorical comparisons as appropriate. Standardized mean differences were calculated using Cohen's d to quantify the magnitude between groups, with values <0.20 considered trivial. A modified Poisson regression was selected to estimate risk ratios (RR), as pregnancy loss is not an uncommon occurrence, and odds ratios may overestimate effect sizes (22). Cluster robust standard errors were estimated at the IVF center level and covariates included oocyte age (year), parity, IVF center, FET protocol (programmed, mNC, and stimulated), blastulation day (day 5, 6, or 7), and Society for Assisted Reproductive Technology (SART) embryo grade (good, fair, poor). The covariates were selected a priori for their known influence on FET outcomes. To reduce the number of covariates, inner cell mass and trophectoderm grades were categorized via the SART simplified embryo scoring system (good = AA or AB, fair = BA, BB or BC, poor = CB, CC or CA) (23). Multicollinearity was assessed using variance inflation factors, and values <10 were considered noncollinear. Subgroup analysis stratified by WHO BMI categories (underweight BMI <18.5 kg/m^2, normal weight BMI 18.5–24.9 kg/m^2, overweight BMI 25.0–29.9 kg/m^2, class I obesity BMI 30.0–34.9 kg/m^2, class II obesity BMI 35.0–39.9 kg/m^2, and class III obesity BMI >40 kg/m^2) were performed using the normal-weight group as the reference. To further investigate the robustness of the findings in the primary analysis, subgroup and sensitivity analyses were completed to explore the impact of parity, polycystic ovary syndrome (PCOS), serum progesterone, and uterine factor infertility. A formal interaction term between obesity and parity and obesity and age was also assessed to determine whether these variables were effect modifiers. Body mass index was modeled continuously using a quadratic term to account for nonlinearity. Adjusted predicted probabilities of pregnancy loss were estimated across the observed BMI range (13–55 kg/m^2) to identify the lowest predicted probability of pregnancy loss.

A post hoc power calculation was performed to assess the magnitude of the effect this study was powered to detect, given the known and predetermined sample size. Statistical analyses were performed using STATA 18 (StataCorp).

RESULTS

Participants and descriptive data

A total of 14,990 patients were included: 11,179 in the nonobese group (74.6%) and 3,811 in the obese group (25.4%). Of the nonobese patients, patients in the normal-weight group comprised the largest proportion (60.8%), followed by overweight (36.6%) and underweight (2.7%). Of the obese group, patients with class 1 obesity made up a significant proportion of patients (56.2%), followed by class 2 (31.2%) and class 3 (12.5%). See the inclusion flow chart in Supplemental Figure 1 (available online).

Patients with obesity had older oocyte age, maternal age at FET, paternal age, and higher BMI. FET protocols and primary diagnoses were statistically significantly different, with a higher proportion of patients with obesity diagnosed with PCOS and a lower proportion undergoing mNC FETs. Serum P4 and E2 levels, endometrial thickness before ovulation or exogenous P4 start, as well as closest to FET, and SART embryo grades were statistically significantly different but clinically similar between groups. Parity, antimüllerian hormone (AMH) levels, and blastulation day were comparable, see Table 1.

Main results

Univariate analyses found statistically significant differences across all pregnancy outcomes (Supplemental Fig. 2), including a lower proportion of biochemical loss (44.2%) and a higher proportion of clinical pregnancy loss (55.9%) in obese patients compared with nonobese patients (52% and 48.0%). The overall mean variance inflation factor (1.99) indicated minimal collinearity. In the adjusted model, no significant differences in the probability of implantation (adjusted risk ratio [aRR]: 0.98, 95% confidence interval [CI] 0.97–1.0, P = .09) or ectopic pregnancy (aRR: 1.09, 95% CI 0.86–1.37, P = .47) were found between groups. Patients with obesity demonstrated a significantly lower probability of clinical (aRR: 0.96, 95% CI 0.94–0.99, P = .002) and ongoing pregnancy (aRR: 0.94, 95% CI 0.92–0.96, P < .001) as well as live birth (aRR: 0.92, 95% CI 0.91–0.94, P < .001). Patients with obesity had a 19% increased risk of pregnancy loss (aRR: 1.19, 95% CI 1.14–1.24, P < .001) compared with their nonobese counterparts (Fig. 1). The adjusted absolute risk difference between groups is 3.1 percentage points (15.9% nonobese vs. 19.5% obese, 95% CI 2.3–3.9) or three additional pregnancy losses per 100 FETs in patients with obesity. Formal interaction testing demonstrated age was not a significant effect modifier (P for interaction = .19),

TABLE 1

Baseline characteristics of patients with obesity and nonobese patients.

	Total n = 14,990	Patients with obesity n = 3,811	Nonobese patients n = 11,179	*P* value (Cohen's d)
Maternal oocyte age (y)	35.1 ± 4.0	35.4 ± 4.1	35.0 ± 4.0	<.001 (−.08)
Body mass index (kg/m^2)	25.4 (22.3–30.1)	34.3 (31.9–37.6)	23.8 (21.5–26.3)	<.001
Antimüllerian hormone (ng/mL)	2.7 (1.4–4.7)	2.7 (1.4–4.8)	2.7 (1.4–4.7)	.36
Parity				
Nulliparous	11,547 (77.0%)	2,963 (77.7%)	8,584 (76.8%)	.22
Parous	3,443 (23.0%)	848 (22.3%)	2,595 (23.2%)	
Paternal age (y)	37.0 ± 5.4	37.2 ± 5.4	36.9 ± 5.4	.02 (–.04)
Primary infertility diagnosis				<.001
DOR	2,648 (16.6%)	643 (16.9%)	2,005 (17.9%)	
Endometriosis	593 (4.0%)	113 (3.0%)	480 (4.3%)	
Fertility preservation	378 (2.5%)	66 (1.7%)	312 (2.8%)	
Genetic	59 (0.4%)	10 (0.3%)	49 (0.4%)	
Male factor	4,510 (30.1%)	1,019 (26.7%)	3,491 (31.2%)	
Obesity	46 (0.3%)	46 (1.2%)	0 (0.0%)	
Other	911 (6.1%)	238 (6.2%)	673 (6.0%)	
Ovulatory dysfunction	1,197 (8.0%)	367 (9.6%)	830 (7.4%)	
PCOS	1,488 (9.9%)	617 (16.2%)	871 (7.8%)	
Tubal factor	1,024 (6.8%)	294 (7.7%)	730 (6.5%)	
Unexplained	1,744 (11.6%)	288 (7.6%)	1,456 (13.0%)	
Uterine factor	392 (2.6%)	110 (2.9%)	282 (2.5%)	
Maternal age at FET (y)	35.5 ± 4.1	35.7 ± 4.1	35.4 ± 4.0	<.001 (−.08)
Days from BMI to FET	142.9 ± 85.6	139.5 ± 85.3	144.1 ± 85.6	.015 (.05)
FET protocol type				
Modified natural	2,691 (18.0%)	432 (11.3%)	2,259 (20.2%)	<.001
Programmed	11,673 (77.9%)	3,247 (85.2%)	8,426 (75.4%)	
Stimulated	626 (4.2%)	132 (3.5%)	494 (4.4%)	
Maximum endometrial thickness (mm)	9.0 (8.0–10.3)	9.2 (8.2–10.6)	8.9 (8.0–10.2)	<.001
Maximum estradiol before ovulation or exogenous progesterone (pg/mL)	243.3 (181.5–338.0)	240.0 (178.3–327.0)	244.3 (182.1–341.7)	.007
Maximum progesterone before ovulation or exogenous progesterone (ng/mL)	0.4 (0.2–0.5)	0.3 (0.2–0.4)	0.4 (0.3–0.5)	<.001
Endometrial thickness closest to FET (mm)	9.7 (8.3–11.3)	9.8 (8.4–11.5)	9.6 (8.3–11.3)	<.001
Serum estradiol closest to FET (pg/mL)	167.0 (120.2–243.0)	176.0 (126.0–252.8)	164.1 (119.0–238.0)	<.001
Serum progesterone closest to FET (ng/mL)	23.5 (17.5–31.0)	19.8 (15.2–25.5)	24.9 (18.7–32.6)	<.001
Blastulation day				.085
5	6,451 (43.0%)	1,679 (44.1%)	4,772 (42.7%)	
6	8,075 (53.9%)	2,001 (52.5%)	6,074 (54.3%)	
7	464 (3.1%)	131 (3.4%)	333 (3.0%)	
SART embryo grade				
Good	7,672 (51.2%)	1,883 (49.4%)	5,789 (51.8%)	.027
Fair	6,590 (44.0%)	1,746 (45.8%)	4,844 (43.3%)	
Poor	728 (4.9%)	182 (4.9%)	546 (4.9%)	
WHO BMI categories				
Underweight	299 (2.0%)	0 (0.0%)	299 (2.7%)	<.001
Normal weight	6,792 (45.3%)	0 (0.0%)	6,792 (60.8%)	
Overweight	4,088 (27.3%)	0 (0.0%)	4,088 (36.6%)	
Class 1 obesity	2,143 (14.3%)	2,143 (56.2%)	0 (0.0%)	
Class 2 obesity	1,190 (7.9%)	1,190 (31.2%)	0 (0.0%)	
Class 3 obesity	478 (3.2%)	478 (12.5%)	0 (0.0%)	

Note: Data are presented as mean (SD) or median (IQR) for parametric and nonparametric continuous variables, respectively, and number (n) (%) for categorical variables. Standardized mean differences (Cohen's d) were calculated for continuous variables, and values (d <0.20) were considered trivial differences between groups. BMI = body mass index; DOR = diminished ovarian reserve; FET = frozen embryo transfer; IQR = interquartile range; PCOS = polycystic ovary syndrome; SART = Society for Assisted Reproductive Technology; WHO = World Health Organization.

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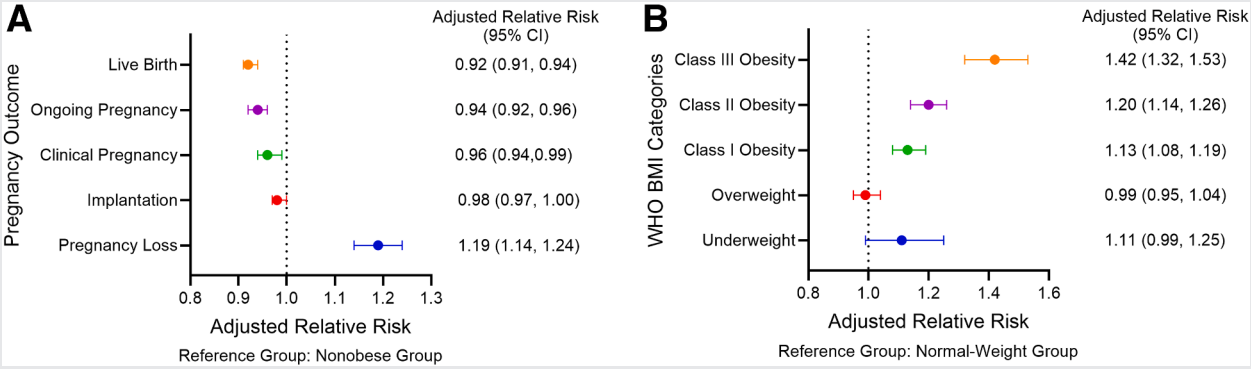
indicating that the relationship between obesity and pregnancy loss did not differ across ages.

Other analyses

Univariate comparisons of pregnancy outcomes across WHO BMI categories showed statistically significant differences (Supplemental Fig. 3). As depicted in Figure 1, when stratified by WHO BMI categories, patients who were categorized as underweight or overweight did not differ significantly from the normal-weight group regarding risk of pregnancy loss (aRR: 1.11, 95% CI 0.99–1.25, $P = .06$ and aRR: 0.99, 95% CI 0.95–1.04, $P = .77$, respectively). However, patients in class I and class II obese groups were associated with a 13% and 20% increased risk of loss compared with the normal-weight group (aRR: 1.13, 95% CI 1.08–1.19, $P < .001$ and aRR: 1.20, 95% 1.14–1.26, $P < .001$). Finally, patients in the class III obesity category (BMI >40.0 kg/m^2) had a 42% increased risk of pregnancy loss compared with the normal-weight group (aRR: 1.42, 95% CI 1.32–1.53,

FIGURE 1



Adjusted relative risk of pregnancy outcomes by obesity status and WHO BMI categories. (**A**). represents the adjusted relative risk of pregnancy outcomes of patients with obesity compared with nonobese patients (reference group). (**B**). represents the adjusted relative risk of pregnancy loss stratified by WHO BMI categories compared with the normal-weight group (reference group). *Adjusted for oocyte age, parity, IVF center, FET protocol, blastulation day, and SART embryo grade. BMI = body mass index; CI = confidence interval; FET = frozen embryo transfer; IVF = in vitro fertilization; SART = Society for Assisted Reproductive Technology; WHO = World Health Organization.

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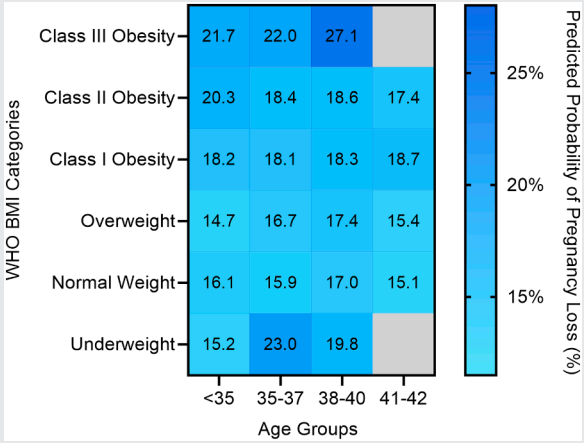
$P < .001$). Compared with normal-weight patients, patients with class I, II, and III obesity were associated with adjusted absolute increases of 2.2 (95% CI 1.3–3.0), 3.2 (95% CI 2.3–4.1), and 6.7 (95% CI 5.1–8.3) percentage points, corresponding to approximately 2, 3, and 7 additional pregnancy losses per 100 embryo transfers, respectively. A heatmap (Fig. 2) illustrates the predicted probability of pregnancy loss across age strata and WHO BMI categories.

Patients with a history of a prior live birth (N = 3,443) had no difference in the probability of loss among patients with and without obesity (aRR 0.90, 95% CI 0.79–1.02, $P = .09$). However, nulliparous patients (N = 11,547) with obesity experienced a 28% increased risk of loss (aRR 1.28, 95% CI 1.24–1.33, $P < .001$) compared with nonobese, nulliparous patients. Formal interaction testing demonstrated parity as a significant effect modifier (P for interaction $< .001$), indicating that the relationship between obesity and loss differed between parous and nulliparous patients. Furthermore, when excluding patients with PCOS (N = 1,448), the results were similar to those of the primary analysis, demonstrating an increased probability of loss (aRR 1.16, 95% CI 1.11–1.22, $P < .001$). When excluding uterine factor infertility (N = 392), patients with obesity performed similarly as those in the primary analysis with an increased risk of loss (aRR 1.20, 95% CI 1.15–1.25, $P < .001$). In the sensitivity analysis, including serum P4 closest to transfer, the results were unchanged (aRR 1.21, 95% CI 1.15–1.27, $P < .001$) and P4 was not independently associated with the outcome. When treating BMI as a continuous variable, a statistically significant nonlinear relationship was observed ($P < .001$), and the predicted risk of loss was lowest at a BMI of 25.3 kg/m^2 (95% CI: 24.3–26.3, $P < .001$). Risk increased at both lower and higher BMI values (Fig. 3).

Post hoc power analysis demonstrated that the fixed sample size provided 99.9% power to detect the differences in magnitude observed between obese and nonobese patients (3.6% difference, 19.5% vs. 15.9%; RR = 1.22).

FIGURE 2



Heat map of predicted probabilities of pregnancy loss by age and WHO BMI category. Heat map of model-predicted probabilities of pregnancy loss across age strata and WHO BMI categories. Predicted probabilities were estimated from the full regression model. Color intensity increases with higher predicted probabilities of pregnancy loss. Cells with fewer than five loss events were censored. BMI = body mass index; WHO = World Health Organization.

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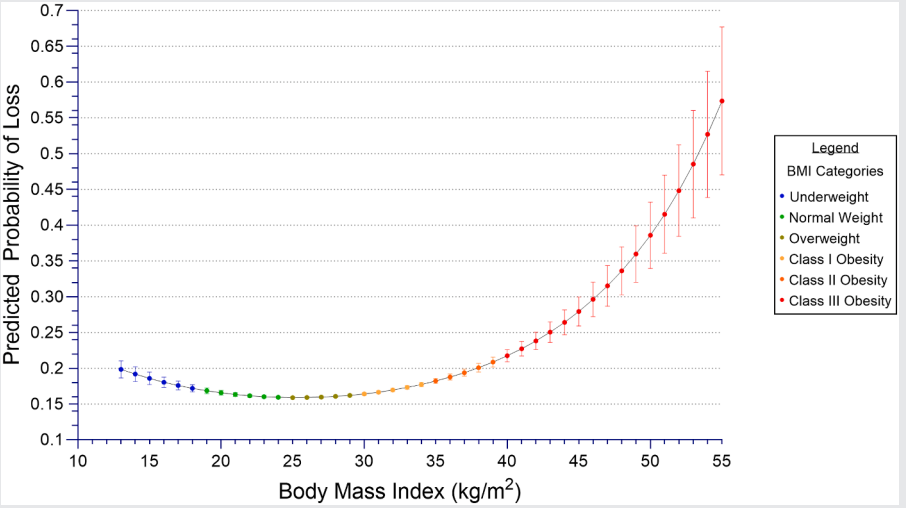
DISCUSSION

Our results demonstrate that patients with obesity have an increased risk of pregnancy loss after single euploid FET compared with patients without obesity, albeit attenuated in parous patients. Although the adjusted relative risk is higher between groups, there is a moderate absolute difference overall. The probability of loss increased progressively with rising BMI, suggesting a dose-dependent effect. When

FIGURE 3



Predicted probability of pregnancy loss across the observed BMI (kg/m^2) spectrum. Predicted probabilities were estimated from the fully adjusted Poisson regression model, including a quadratic BMI term. Confidence intervals are wider at the higher BMI values (BMI >45 kg/m^2) due to an overall lower number of observations. BMI = body mass index.

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stratified by WHO BMI categories, the risk of loss increased in a stepwise fashion, and the absolute risk incrementally increased with advancing obesity classes.

Although our findings differ from earlier studies that reported no differences in outcomes for patients with obesity, they are more consistent with recent evidence where IVF patients with obesity experience adverse reproductive outcomes (5, 7, 8, 16, 24, 25). Earlier work may reflect heterogeneous practices, older technologies and techniques, participant bias, smaller samples, unequal BMI category distributions, and varying obesity definitions. For example, Prost et al. (16), determined that obesity does not impact live birth rates; however, they did not control for aneuploidy, included ≥ 1 embryo(s) transferred and compared only patients of normal weight with those with obesity. Insogna et al. (26) reported a neutral effect of BMI on implantation; however, they utilized slow freezing and thawing methods, which may impair embryo survival and potential, and primarily compared overweight women with normal-weight women because of low numbers of patients with obesity, which may have limited statistical power. Maternal age is a well-established determinant of reproductive success, and prior work by Goldman et al. (27) demonstrated that increasing age was more influential than BMI on live birth in cycles without PGT-A. In contrast, our study included euploid transfers, minimizing age-related aneuploidy. Notably, Goldman et al. (27) found an association with higher BMI and lower live birth rates in younger ages, where age-related aneuploidy is less of a factor. Recently, Lawrenz et al. (28) demonstrated that BMI was associated with miscarriage in euploid FETs, independent of age, supporting our findings. Collectively, these data allow for nonaneuploidy-related prognostic factors to be assessed. Lastly, the prospective cohort study performed by Kim et al. (8) may be limited by volunteer bias.

Despite a smaller sample size, older oocyte age, and a leaner population, our results are similar to Cozzolino et al. (24), who found female obesity increases the miscarriage risk of euploid embryos. Similarly, Bellver et al. (7) found higher rates of miscarriage in patients with obesity undergoing euploid FET (7). Overall, our findings align with contemporary evidence suggesting that obesity may exert clinically meaningful and statistically significant effects on IVF outcomes, including pregnancy loss. Although absolute differences are smaller than relative risks, even incremental differences in pregnancy loss may be relevant to patients and providers because pregnancy loss often causes further consequences, including emotional anguish, additional treatment, delays, and dropout (29). This overarching evidence suggests that although patients with obesity may obtain euploid embryos for transfer, the untoward effect of obesity is not entirely eliminated. This may be reflective of maternal factors including chronic inflammation, insulin resistance, impaired decidualization or alterations in P4 pharmacokinetics or endometrium, which may impair implantation and pregnancy maintenance, despite euploid FET (30–32).

To further explore and validate our findings, sensitivity analyses evaluated the impact of PCOS and uterine factor infertility. Excluding patients with PCOS reduced confounding because PCOS has been associated with a higher baseline risk of loss (5). Bakkensen et al. (5) performed subgroup analyses among patients with PCOS, comparing those with and without obesity, and found that patients with obesity had an increased probability of pregnancy loss. In our sensitivity analysis, the association between obesity and loss remained similar, regardless of PCOS diagnosis, suggesting that our findings are not PCOS dependent. In parallel, these findings suggest

that obesity is independently associated with pregnancy loss.

Uterine factor diagnoses are associated with adverse IVF outcomes; however, only fibroids and endometrial hyperplasia are linked with obesity (33–41). To isolate the impact of obesity on loss, we conducted sensitivity analyses excluding patients with uterine factor and found similar results. The relationship between obesity and loss remained, regardless of the uterine factor. Consequently, in otherwise anatomically normal uteri, our data demonstrate that obesity may exert a distinct effect on pregnancy loss after euploid FET.

The role of parity as a prognostic factor in IVF outcomes is incompletely characterized. Most available evidence is derived from RPL literature, which suggests that parous women with RPL have a better prognosis to reach live birth in subsequent pregnancies than nulliparous women (42–44). In our study, nulliparous patients with obesity experienced a similarly elevated risk of loss as observed in the primary analysis. In contrast, this association was attenuated among parous patients (i.e., secondary infertility), suggesting that prior live birth may mitigate the adverse effect of obesity on loss. Consistent with RPL research, parity may represent a more favorable prognosticator independent of BMI.

As BMI was measured proximal to FET, we cannot determine BMI status at the time of prior pregnancy or the impact of interpregnancy changes. Importantly, we evaluated only euploid FETs, therefore the observed differences are less likely to reflect embryonic aneuploidy and may instead be attributable to other maternal factors. Furthermore, the history of a prior uncomplicated live birth may reflect a favorable maternal environment, thus attenuating risk factors like obesity (45, 46). Our findings are consistent with the broader obstetrical data demonstrating the association between prior uncomplicated live birth and lower risk in subsequent pregnancies (45, 46).

Strengths of this study include its large sample size and inclusion of multiple IVF centers enhancing generalizability. Pregnancy loss was selected as the primary outcome, an understudied endpoint in prior IVF research, despite being a major contributor to treatment discontinuation (29). The use of contemporary, standardized practices, including the first autologous euploid blastocyst FET, lessens residual confounding. Incorporation of PGT-A reduced losses attributable to aneuploidy, further isolating the association between obesity and loss. The use of a comprehensive EMR enabled robust data capture, particularly for covariates, reducing bias from missing data and strengthening internal validity. Unlike studies that select covariates on the basis of post hoc analyses, covariates in this analysis were defined a priori on the basis of biologic plausibility and established clinical relevance. In using retrospective data, this study may reduce volunteer bias that occurs with prospective study enrollment.

Several limitations merit consideration. As with all retrospective studies, residual confounding cannot be excluded, and some potentially relevant demographic (i.e., ethnicity and menstrual regularity) and metabolic variables (i.e., history of smoking, hypertension, diabetes or thyroid disease) were not available. Given the large sample size, small differences between groups may reach statistical significance without representing clinical relevance. The study population may represent a more favorable prognosis, as all patients had at least one autologous, euploid blastocyst available, which may limit generalizability to broader populations. Although confounding due to chromosomal copy number is reduced by PGT-A, other embryonic factors affecting implantation may not have been eliminated. Analyses were limited to BMI, as alternative measures of body habitus are not collected. Consequently, other anthropometric indices, which may reflect a better measurement of metabolic health, such as waist-to-hip ratio or body fat percentage, were not evaluated.

Future research identifying clinically relevant measures of body habitus that best reflect maternal health and predict outcomes is needed, including the optimal timing and standardization of these measurements. Importantly, prospective studies evaluating weight loss interventions are warranted. Emerging pharmacologic therapies, such as glucagon-like peptide-1receptor agonists, should be explored to understand effects and potential risks, including rebound weight gain.

CONCLUSION

Patients with obesity undergoing euploid FET have a statistically significant increased risk of early pregnancy loss compared with nonobese patients. Risk rises with increasing BMI and worsening BMI categories. It is crucial that patients with obesity receive appropriate counseling regarding their risk of loss. Although the availability of euploid embryos is often viewed as a pregnancy loss reduction strategy, euploidy does not fully mitigate the risk of adverse pregnancy outcomes, particularly among patients with obesity. The burden of pregnancy loss is substantial and may contribute to treatment discontinuation, thereby reducing the likelihood of achieving a successful outcome. These findings underscore the importance of counseling patients before euploid FET regarding the impact of obesity on early pregnancy loss.

CRediT Authorship Contribution Statement

Christine Whitehead: Writing – review & editing, Writing – original draft, Validation, Methodology, Formal analysis, Data curation, Conceptualization. **Kristin Lefebvre:** Writing – review & editing, Methodology, Conceptualization. **Emre Seli:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of Interests

C.W. has nothing to disclose. K.L. has nothing to disclose. E.S. has nothing to disclose.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be found online at https://doi.org/10.1016/j.fertnstert.2026.04.016.

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La obesidad se asocia con un mayor riesgo de pérdida temprana del embarazo tras la transferencia de embriones congelados euploides.

Objetivo: Determinar si la obesidad está asociada con un mayor riesgo de pérdida del embarazo en pacientes que se someten a transferencia autóloga de embriones congelados euploides (FET).

Diseño: Estudio de cohorte retrospectivo.

Sujetos: Se incluyeron pacientes con índice de masa corporal (IMC) registrado de nueve centros clínicos entre enero de 2019 y diciembre de 2024, que se sometieran a su primer TEC autólogo único y euploide. Se excluyeron otras indicaciones de pruebas genéticas pre implantacionales.

Exposición: Los pacientes se estratificaron en dos grupos: pacientes con obesidad (IMC $\geq$30,0 kg/m2) y pacientes no obesos (IMC $<$30,0 kg/m2).

Principales medidas de resultado: El resultado principal fue la pérdida bioquímica del embarazo (beta gonadotropina coriónica humana [ß-hCG] $>$5 mIU/mL sin evidencia de ecografía de embarazo hasta ß-hCG $<$5 mIU/mL) o pérdida clínica del embarazo (evidencia ecografía de al menos un saco gestacional intrauterino, que no progresó a nacimiento vivo). Los resultados secundarios incluyeron implantación, embarazo ectópico, clínico y en curso (8–9 semanas de edad gestacional con actividad cardíaca) y nacimiento vivo (neonato $>$24 semanas de edad gestacional).

Resultados: Se incluyeron un total de 14.990 pacientes: 11.179 no obesos y 3.811 con obesidad. En comparación con los no obesos, los pacientes con obesidad eran mayores. La paridad, los niveles de hormona antimulleriana (AMH) y el día de la blastulación fueron similares entre los grupos. Tras el ajuste, las pacientes con obesidad tuvieron un 19% más de riesgo de pérdida del embarazo (riesgo relativo ajustado [aRR]: 1,19, intervalo de confianza [IC] 95%: 1,14–1,24) en comparación con no obesas. Cuando se estratifican por categorías de IMC, las obesidades de clase I (IMC 30,0–34,9 kg/m2), II (IMC 35,0–39,9 kg/m2) y III (IMC $\geq$40,0 kg/m2) tuvieron un riesgo incrementado del 13%, 20% y 42% de pérdida del embarazo, respectivamente, mientras que los grupos con bajo peso (IMC $<$18,0 kg/m2) y sobrepeso (IMC 25,0–29,9 kg/m2) tuvieron un desempeño similar al grupo de peso normal (IMC 18,5–24,9 kg/m2). La más baja probabilidad predictiva de aborto se obtuvo con un IMC de 25,3 kg/m2. Aunque no hubo diferencias en la implantación (aRR: 0,98, IC 95% 0,86–1,37), las pacientes con obesidad tuvieron menores probabilidades de embarazo clínico (aRR: 0,96, IC 95%: 0,94–0,99) de embarazo en curso (aRR: 0,94, IC 95% 0,92–0,96) y de nacimientos vivos (aRR: 0,92, IC 95%: 0,91–0,94). El riesgo de pérdida del embarazo se atenuó en pacientes multíparas con obesidad (aRR: 0,90, IC 95% 0,79–1,02).

Conclusión: Considerando la aneuploidía embrionaria en el contexto de transferencias solo euploides, las pacientes con obesidad tuvieron un 19% más riesgo de pérdida precoz del embarazo en comparación con las no obesas, aumentando el riesgo a medida que aumentan las categorías de IMC.