Reproductive outcomes following insemination in same-sex female couples, unpartnered female patients, and heterosexual couples

Same-sex female couples and unpartnered female patients are now relying more often on fertility services, specifically therapeutic donor insemination (TDI), as a means of family building. However, data are limited on TDI outcomes in these groups compared with intrauterine insemination (IUI) outcomes in heterosexual couples, which becomes problematic when counseling these groups (1–5). Moreover, another challenge facing providers is determining when to proceed to in vitro fertilization (IVF) after multiple cycles of TDI or IUI have been unsuccessful. Therefore, the objective of this study was to investigate TDI outcomes in same-sex female couples and unpartnered female patients as well as IUI outcomes in heterosexual couples.

MATERIALS AND METHODS

Study design

This retrospective cohort study was conducted at an academically affiliated fertility center, Boston IVF, in the northeastern United States. Patient demographics, cycle characteristics, and cycle outcomes were extracted from the electronic medical records of all same-sex female couples and unpartnered female patients undergoing a TDI cycle, and all heterosexual couples undergoing an IUI cycle using autologous sperm from January 1, 2017, to December 31, 2021. Further details regarding the stimulation protocol are available in the Supplemental Methods section (available online).

The primary outcome was the cumulative incidence of the first clinical pregnancy after up to 10 insemination cycles. Clinical pregnancy was defined as the presence of a gestational sac or other clinical features of a pregnancy confirmed on ultrasound. The cumulative incidence of the first clinical pregnancy was calculated as the number of patients in the group of interest who experienced a clinical pregnancy up to and including the cycle of interest divided by the total number of patients in the group. In addition, the cumulative incidence of the first clinical pregnancy through up to six cycles of IUI was also stratified by age (<38 and ≥38 years) and body mass index (BMI; <25, 25 to <30, and ≥30 kg/m^2). Supplemental calculations including 95% binomial confidence intervals (CIs) using the Wilson score interval were also completed for the aforementioned data points. Furthermore, generalized estimating equations were used to estimate the risk ratios and 95% CIs of the outcomes in each of the stratified age and BMI groups. Finally, all data analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and GraphPad Prism (GraphPad Software for Windows, La Jolla, CA).

RESULTS

In total, 795 same-sex female couples completing 2,713 TDI cycles, 355 unpartnered female patients completing 1,160 TDI cycles, and 4,014 heterosexual couples completing 9,870 IUI cycles during the 5-year period were included in the analysis. Details regarding patient demographics and cycle characteristics are illustrated in Table 1.

In terms of outcomes, 239 (30.1%; 95% CI, 27.0–33.3) same-sex female couples, 80 (22.5%; 95% CI, 18.5–27.2) unpartnered female patients, and 720 (17.9%; 95% CI,

TABLE 1

Baseline patient demographics and cycle characteristics by group.

Patient demographics	Heterosexual couples n = 4,014 couples	Same-sex female couples n = 795 couples	Unpartnered female patients n = 355 patients
Age (y)	33.5 ± 4.0	32.9 ± 4.1	37.4 ± 4.7
Body mass index (kg/m^2)	27.7 ± 7.2	28.8 ± 6.7	28.7 ± 6.6
Antimüllerian hormone (ng/mL)	3.7 ± 3.8	3.3 ± 2.5	2.4 ± 3.1
Cycle characteristics	**Heterosexual couples N = 9,870 cycles**	**Same-sex female couples N = 2,713 cycles**	**Unpartnered female patients N = 1,160 cycles**
Baseline follicle-stimulating hormone (mIU/mL)	7.3 ± 4.0	7.1 ± 3.0	7.9 ± 3.7
Baseline estradiol (pg/mL)	44.8 ± 37.8	41.5 ± 41.3	45.0 ± 40.3
No. of medicated IUIs	9,124 (92%)	1,246 (46%)	622 (54%)
Peak estradiol (pg/mL)	383.3 ± 347.8	299.8 ± 288.1	408.9 ± 288.1
No. of ovarian follicles ≥16 mm	1.5 ± 0.7	1.4 ± 0.6	1.4 ± 0.9
Total motile sperm in the semen sample (mil)	24.2 ± 6.5	14.1 ± 2.6	14.2 ± 1.2

Note: Data are shown as means ± standard deviations or numbers (percentages). IUI = intrauterine insemination.

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TABLE 2

Cycle-specific and cumulative incidence of clinical pregnancy by group among all patients.

	Heterosexual couples n = 4,014 couples			Same-sex female couples n = 795 couples			Unpartnered female patients n = 355 patients		
Cycle	Started cycle	Cycle-specific clinical pregnancy	Cumulative clinical pregnancy	Started cycle	Cycle-specific clinical pregnancy	Cumulative clinical pregnancy	Started cycle	Cycle-specific clinical pregnancy	Cumulative clinical pregnancy
1	4,014	376 (9.4, 8.4–10.3)	376 (9.4, 8.4–10.3)	795	81 (10.2, 8.3–12.5)	81 (10.2, 8.3–12.5)	355	34 (9.0, 6.9–13.1)	34 (9.0, 6.9–13.1)
2	2,779	222 (8.0, 7.0–9.1)	598 (14.9, 13.8–16.0)	606	55 (9.1, 7.0–11.6)	136 (17.1, 14.7–19.9)	267	21 (7.9, 5.2–11.7)	55 (15.5, 12.1–19.6)
3	1,414	82 (5.8, 4.7–7.1)	680 (16.9, 15.8–18.1)	447	41 (9.2, 6.8–12.2)	177 (22.3, 19.5–25.3)	193	8 (4.1, 2.1–8.0)	63 (17.7, 14.1–22.1)
4	394	26 (6.6, 4.5–9.5)	706 (17.6, 16.4–18.8)	275	28 (10.2, 7.1–14.3)	205 (25.8, 22.9–28.9)	126	9 (7.1, 3.8–13.0)	72 (20.3, 16.4–24.8)
5	157	10 (6.4, 3.5–11.3)	716 (17.8, 16.7–19.1)	188	16 (8.5, 5.3–13.4)	221 (27.8, 24.8–31.0)	85	0 (0.0, 0.0–4.3)	72 (20.3, 16.4–24.8)
6	77	4 (5.2, 2.0–12.6)	720 (17.9, 16.7–19.2)	137	13 (9.5, 5.6–15.6)	234 (29.4, 26.4–32.7)	60	7 (11.7, 5.8–22.2)	79 (22.3, 18.2–26.9)
7	16	0 (0.0, 0.0–19.4)	720 (17.9, 16.7–19.2)	35	4 (11.4, 4.5–26.0)	238 (29.9, 26.9–33.2)	9	1 (11.1, 2.0–43.5)	80 (22.5, 18.5–27.2)
8	4	0 (0.0, 0.0–49.0)	720 (17.9, 16.7–19.2)	16	0 (0.0, 0.0–19.4)	238 (29.9, 26.9–33.2)	5	0 (0.0, 0.0–43.5)	80 (22.5, 18.5–27.2)
9	2	0 (0.0, 0.0–65.8)	720 (17.9, 16.7–19.2)	9	1 (11.1, 2.0–43.5)	239 (30.1, 27.0–33.3)	2	0 (0.0, 0.0–65.8)	80 (22.5, 18.5–27.2)
10	0	—	—	7	0 (0.0, 0.0–35.4)	239 (30.1, 27.0–33.3)	0	—	—

Note: Data are shown as numbers (percentages and 95% confidence intervals).

Heyward. Reproductive outcomes after insemination. Fertil Steril 2025.

16.7–19.2) heterosexual couples achieved a clinical pregnancy after up to 10 cycles of TDI or IUI. However, among the patients and couples who were successful in achieving a clinical pregnancy, 205 (85.8%; 95% CI, 80.8–89.6) same-sex female couples, 72 (90.0%; 95% CI, 81.5–94.9) unpartnered female patients, and 706 (98.1%; 95% CI, 96.8–98.8) heterosexual couples attained their first clinical pregnancy within four treatment cycles (Table 2).

When stratifying by age, the cumulative clinical pregnancy rates were noted to be significantly higher in those aged <38 years than in those aged ≥38 years among both same-sex female couples (P=.01) and heterosexual couples (P=.002); however, this observation was not seen when comparing the cumulative clinical pregnancy rates among unpartnered female patients (P=.08) as shown in Supplemental Table 1 (available online). However, analogous to the general cohort, trends persisted in both stratified age ranges given that the vast majority of patients had their first clinical pregnancy within four TDI or IUI cycles (Supplemental Tables 2 and 3).

Lastly, patients within each group were also stratified by BMI. Conversely to the age trends, there was no clear pattern of worsened outcomes with increasing BMI level. On the basis of the results in Supplemental Table 1, aside from a significantly higher cumulative clinical pregnancy rate among heterosexual couples with an overweight BMI than among those with a normal BMI (P=.04), there were no significant differences associated with BMI in any group (all P≥.11). Nevertheless, similar to the general cohort and both stratified age categories, most patients in all three BMI groups achieved their first clinical pregnancy within four insemination cycles (Supplemental Tables 4–6).

CONCLUSION

This study has demonstrated that TDI is a viable and effective option for achieving a clinical pregnancy in same-sex female couples and unpartnered female patients, which is essential given the lack of data demonstrating the effectiveness of insemination in these groups. However, as with IUI in heterosexual couples, TDI in same-sex female couples and unpartnered female patients should be limited to four cycles given the minimal benefit of pursuing additional cycles. It is the hope that the results of this study be used as a guide for clinicians in their approach to treating these groups. After four cycles, providers should reevaluate a patient's treatment and consider a more aggressive approach such as IVF to optimize their chances of a successful pregnancy.

CRediT Authorship Contribution Statement

Quetrell D. Heyward: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Denis A. Vaughan:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Conceptualization. **Laura E. Dodge:** Writing – review & editing, Methodology, Formal analysis. **Daniel Duvall:** Methodology, Data curation. **Denny Sakkas:** Writing – review & editing, Validation, Supervision, Investigation, Conceptualization. **Riwa Sabbagh:** Writing – review & editing, Conceptualization. **Ann K. Korkidakis:** Writing – review & editing, Conceptualization. **Alan S.**

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Declaration of Interests

Q.D.H. has nothing to disclose. D.A.V. has nothing to disclose. L.E.D. has nothing to disclose. D.D. Jr. has nothing to disclose. D.S. has previously spoken on panels sponsored by EMD Serono, has stock options in Alife and Rita Health, and is on the advisory board of Legacy. R.S. has nothing to disclose. A.K.K. has nothing to disclose. A.S.P. has nothing to disclose.

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REFERENCES

1. Johal JK, Gardner RM, Vaughn SJ, Jaswa EG, Hedlin H, Aghajanova L. Pregnancy success rates for lesbian women undergoing intrauterine insemination. F S Rep 2021;2:275–81.
2. Nazem TG, Chang S, Lee JA, Briton-Jones C, Copperman AB, McAvey B. Understanding the reproductive experience and pregnancy outcomes of lesbian women undergoing donor intrauterine insemination. LGBT Health 2019;6:62–7.
3. Hochberg A, Dahan MH, Dinh T, Buckett W, Ruiter-Ligeti J. A low total motile sperm count in donor sperm obtained from commercial banks does not affect pregnancy rates from intrauterine insemination. Eur J Obstet Gynecol Reprod Biol X 2023;21:100267.
4. Soares SR, Cruz M, Vergara V, Requena A, García-Velasco JA. Donor IUI is equally effective for heterosexual couples, single women and lesbians, but autologous IUI does worse. Hum Reprod 2019;34:2184–92.
5. Linara-Demakakou E, Bodri D, Wang J, Arian-Schad M, Macklon N, Ahuja K. Cumulative live birth rates following insemination with donor spermatozoa in single women, same-sex couples and heterosexual patients. Reprod Biomed Online 2020;41:1007–14.