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Tubal Factor Infertility, In Vitro Fertilization, and Racial Disparities: A Retrospective Cohort in Two US Clinics

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Abstract

Background: Nearly 14% of US women report any lifetime infertility which is associated with health care costs and psychosocial consequences. Tubal factor infertility (TFI) often occurs as a result of sexually transmitted diseases and subsequent pelvic inflammatory disease. We sought to evaluate for and describe potential racial disparities in TFI and in vitro fertilization (IVF) prevalence.

Methods: Records of women aged 19 to 42 years in our retrospective cohort from 2 US infertility clinics were reviewed. We calculated TFI prevalence, IVF initiation prevalence, and prevalence ratios (PRs), with 95% confidence intervals (CIs) for each estimate, overall and by race.

Results: Among 660 infertile women, 110 (16.7%; 95% CI, 13.8–19.5%) had TFI which was higher in Black compared with White women (30.3% [33/109] vs 13.9% [68/489]; PR, 2.2 [95% CI, 1.5–3.1]). For women with TFI, IVF was offered to similar proportions of women by race (51.5% [17/ 33] vs 52.9% [36/68] for Black vs White women); however, fewer Black than White

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women with TFI started IVF (6.7% [1/15] vs 31.0% [9/29]; PR, 0.2 [95% CI, 0–1.0]), although the difference was not statistically different.

Conclusions: Tubal factor infertility prevalence was 2-fold higher among Black than White women seeking care for infertility. Among women with TFI, data suggested a lower likelihood of Black women starting IVF than White women. Improved sexually transmitted disease prevention and treatment might ameliorate disparities in TFI.

Tubal factor infertility (TFI) results from obstruction of 1 or both fallopian tubes and is caused by bacterial sexually transmitted infections (STIs), including chlamydia and gonorrhea. *Chlamydia trachomatis*, *Neisseria gonorrhoeae,* and other microorganisms can ascend from the cervix to the upper genital tract and cause pelvic inflammatory disease (PID), which may cause fallopian tubal scarring and dysfunction. Up to 15% to 20% of women with PID subsequently develop infertility.[1] Pelvic inflammatory disease and resulting tubal damage also increase the risk of ectopic pregnancy. A large proportion of post-PID infertility is caused by TFI[2] which accounts for up to one-third of all female infertility.[3–5] Tubal factor infertility may even develop after subclinical PID.[6]

Sexually transmitted infection-related tubal damage may explain TFI. Tubal factor infertility has been reported to be higher in Black compared with White women in a few studies.[7,8] The higher rates of chlamydia and gonorrhea in young Black and Hispanic women aged 20 to 24 years compared with White women[9] and the higher reported likelihood for Black women to develop PID[10,11] support possible racial differences in TFI.

Among US women surveyed about seeking any infertility treatment, 6% of those reporting any medical treatment for infertility reported ever using in vitro fertilization (IVF) or any other form of assisted reproductive technology (ART).[12] In vitro fertilization can be an effective, although costly, treatment option for women with infertility. A single cycle of IVF can cost an average of $12,000[13] in the United States and few states mandate IVF insurance coverage.[14] Because of these costs, IVF is not easily accessible to all women with infertility. Racial disparities have been reported in accessing infertility services[4,7,15,16]; however, prior studies have not always been powered to demonstrate racial differences in use of ART services.[12,15]

Because there are medical costs associated with treating infertility and psychosocial consequences of infertility among women,[17,18] public health efforts have tried to address infertility prevention.[4] There are data about racial disparities in women affected by female infertility; however, less is known about potential contributors to disparities.[15,16,19] We evaluated TFI prevalence and IVF treatment by race among women who presented for care at 2 US infertility clinics to assess for racial disparities in TFI prevalence and IVF treatment and better understand characteristics associated with TFI and IVF.

MATERIALS AND METHODS

We conducted a retrospective cohort study of women aged 19 to 42 years presenting for an initial infertility evaluation at 2 reproductive endocrinology and infertility clinics from January 1, 2011, to June 30, 2012, in Birmingham, Alabama and Pittsburgh, Pennsylvania.

The Birmingham clinic was a private, community-based clinic, whereas the Pittsburgh clinic was university-affiliated.

A random sample of women with all-cause infertility at each clinic was included. We estimated a sample size of 250 patients per clinic assuming a TFI prevalence of 30% among infertile women; however, additional women were included because of a lower overall TFI prevalence assessed after the first group of reviewed charts. Women were excluded if they had history of bilateral tubal ligation. Paper and electronic medical records of women were reviewed and abstracted using a standardized data collection form for the 24-month period starting with the date of each woman's first visit. Separate data abstractors abstracted data at each site. Women with infertility were identified in the IVF surveillance databases at the clinics to obtain complete outcome data.

Definitions

Infertility was defined as the inability to achieve a non-biochemical (spontaneous) intrauterine pregnancy over a 12-month period despite sexual intercourse for women not using contraception. Tubal factor infertility diagnosis was based on any of the following findings: unilateral or bilateral hydrosalpinx on pelvic ultrasound or laparoscopy, any fallopian tube obstruction or occlusion evident on hysterosalpingogram or sonohysterosalpingogram, evidence of fallopian tube damage on laparoscopy (unrecognizable or fragmented fimbriae or tubal fibrosis), tubal occlusion by dye test during laparoscopy, or peritubal or periovarian adhesions in the absence of prior pelvic surgery or endometriosis. Tubal factor infertility was classified as severe if there was bilateral TFI involvement on ultrasound, hysterosalpingogram, sonohysterosalpingogram, or laparoscopy. Unilateral involvement was classified as mild TFI. In vitro fertilization initiation was defined if a woman started IVF based on report in clinic surveillance databases within 2 years of her initial visit. Women for whom IVF was documented as being offered as a treatment option in the medical record were considered to have been offered IVF. In vitro fertilization outcomes were defined as follows based on information obtained within 24 months from each woman's initial visit: intrauterine IVF pregnancy included all women with infertility who had an IVF intrauterine pregnancy and an intrauterine IVF live birth was defined for all women with infertility who had a live birth with IVF. Women with missing IVF outcome were included in the denominator. For analyses by self-reported race which was abstracted from the medical record, women were classified as White if "White" was the only racial category recorded, and as Black if "Black" was recorded as a racial category (including multiracial women for whom "Black" was recorded as a racial category). Women identified as being American Indian, Asian, Pacific Islander uniquely or in any combination other than identifying as Black, were classified in the "other" category. Age was categorized into 19 years to younger than 25 years, 25 years to younger than 35 years, and 35 and older up to and including 42 years.

Analytic Methods

We calculated the TFI prevalence and the 95% Wald CI among all women in the cohort and stratified by race, city in which the clinic was located, and additional characteristics to assess for confounding. For any prevalence estimates with small sample size and a proportion

close to 0 or 1, we calculated Wilson CIs and likelihood ratio prevalence ratio (PR) CIs. We compared TFI prevalence within strata using PR with 95% CI and χ^2 or Fisher exact tests. Among women with TFI, we calculated the proportion with 95% CI of women who started IVF, stratified by race, clinic location, and additional characteristics. We additionally assessed the proportion and 95% Wald CI for all infertile women being offered IVF, starting IVF, having an intrauterine pregnancy, and having a live birth, overall and by race. Missing data were excluded from relevant analyses except as indicated. SAS 9.4 was used for the analyses.

Ethics Approval

Ethics approval was obtained from the University of Alabama at Birmingham and University of Pittsburgh Institutional Review Boards. Centers for Disease Control and Prevention determined that additional research review was not required.

RESULTS

Characteristics of Women and TFI Prevalence

There were 660 infertile women aged 19 to 42 years included in our sample who presented to the 2 clinics over the study period. Among 636 women for whom data on race were reported, 489 (76.9%) were White and 109 (17.1%) were Black (Table 1). Most women were 25 to 34 years of age and a majority (62.0%, n = 409) attended the Birmingham clinic. Among all women, 110 (16.7%, 95% CI, 13.8–19.5%) had TFI. Tubal factor infertility prevalence was higher among: Black (30.3%) than White women (13.9%) (PR, 2.2; 95% CI, 1.5–3.1); women seen in Birmingham (19.6%) compared with those in Pittsburgh (12.0%) (PR, 1.6; 95% CI, 1.1–2.4); women with private insurance (19.0%) compared with those with public insurance (12.6%) (PR, 1.5; 95% CI, 1.0–2.3); and women with prior ectopic pregnancy (45.2%) compared with those without ectopic pregnancy (17.0%) (PR, 2.7; 95% CI, 1.7–4.3) (Table 1).

TFI Epidemiology by Race and City

We calculated TFI prevalence stratified by race and city (Fig. 1 and Supplementary Table 1a and 1b, http://links.lww.com/OLQ/A660) to further explore TFI differences. Among older women, we observed higher TFI prevalences comparing Black to White women (PR, 2.3; 95% CI, 1.5–3.7 for women 25–34 years and PR, 2.1; 95% CI, 1.2–3.7 for women greater than or equal to 35 years). After stratification by race, differences in TFI prevalence by city were not observed. Although 78.9% of Black women and 69.0% of White women had private insurance, few women had insurance coverage for IVF treatment, although this did differ by race (PR, 0.3; 95% CI, 0.1–0.7; comparing Black [5.6%] with White [16.6%] women). Overall, women with private insurance had a higher TFI prevalence than women with public insurance (Table 1), yet this association did not persist after stratification by race (Supplementary Table 1a and 1b, http://links.lww.com/OLQ/A660).

Despite the overall association of ectopic pregnancy history with TFI (PR, 2.7; 95% CI, 1.7–4.3) (Table 1), when stratified by race, this association was found among White (PR, 2.9; 95% CI, 1.6–5.2) but not Black women (PR, 1.6; 95% CI, 0.3–3.5) (Supplemental Tables

1a and 1b, http://links.lww.com/OLQ/A660). Black women without ectopic pregnancy had a high TFI prevalence of 32.0%, 95% CI, 18.6–45.4% (Supplementary Table 1a, http://links.lww.com/OLQ/A660).

Characterizing TFI

Among 105 (of 110) women from who we had TFI severity data, 28.6% had severe TFI. Nearly half of Black women with TFI had severe TFI (48.5%; 95% CI, 30.5–66.5%), whereas only 18.8% (95% CI, 8.9–28.6%) of White women had severe TFI (PR, 2.6; 95% CI, 1.4–4.8). The frequency of severe TFI did not differ between the 2 clinics (23.3% in Pittsburgh vs 30.7% in Birmingham; PR, 0.8; 95% CI, 0.4–1.6).

IVF and Outcomes Among All Women

Data on whether IVF was offered were available for 109 (99.1%) women with TFI, and for 99.6% of women with non-TFI infertility. Among women with TFI and with available data, the proportion offered IVF did not appreciably differ between Black (51.5%) and White (52.9%) women.

For IVF initiation, data were available for 385 (58.3%) women of all with infertility, and for 50 (45.5%) women with TFI. Overall IVF initiation missingness differed by clinic (67.0% for Birmingham and 0.4% for Pittsburgh; PR, 168.2; 95% CI, 38.4–2943.1) and by race (54.1% for Black vs 41.7% for White women; PR, 1.3; 95% CI, 1.1–1.6) although it did not differ by race within each clinic. Among 50 women with TFI, 13 (26.0%; 95% CI, 13.4–38.6%) started IVF (Table 2). The same proportion of women with non-TFI infertility (26.0%) started IVF. A smaller proportion of Black women with TFI started IVF (6.7%) than White women with TFI (31.0%), although the difference was not statistically significant (PR, 0.2; 95% CI, 0–1.0) (Table 2). The prevalence of starting IVF among women with TFI was statistically significantly higher in women with versus without prior ectopic pregnancy history (PR, 3.8; 95% CI, 1.2–15.2) (Table 2).

The IVF outcomes for women with versus without TFI by race are presented in Figures 2A and B. Although a similar proportion of Black and White women with TFI were offered IVF, this differed for women with non-TFI where White women were offered IVF more frequently (Figs. 2A and B). By absolute percentages, IVF outcomes of having an intrauterine pregnancy and a live birth were less frequent in Black than White women regardless of TFI status; however, these outcomes were not statistically different (Fig. 2B).

DISCUSSION

In our retrospective cohort analysis of TFI and IVF utilization in infertility clinics in 2 US states, we used a comprehensive TFI definition and a measure of TFI severity to describe TFI prevalence by race. Beyond an overall TFI prevalence of 16.7%, we found that Black women had a 2-fold higher TFI prevalence than White women among women with infertility. Racial differences persisted by TFI severity, although differences in the absolute proportion of women with TFI starting IVF and with IVF outcomes were not statistically different.

This observed TFI prevalence of 16.7% is similar to or lower than other published estimates. Among other studies of infertile women accessing ART services, 15% to 22% had TFI.[20,21] Higher estimates (25–35%) have been reported particularly when tubal pathology is combined with pelvic or other uterine pathology.[3,5,22]

Previous studies have also observed differences in TFI by race. One study of women seeking infertility care used International classification of diseases-9 infertility codes and found a nearly 5 times higher prevalence for Black versus White women.[7] Among infertile women presenting for ART, TFI was 2 times as prevalent among Black compared with White women, similar to our estimate.[8,15,19]

Pelvic inflammatory disease due to STIs is the most common etiology of TFI,[2,5] and PID can lead to ectopic pregnancy. We found a higher TFI prevalence in women who reported a prior ectopic pregnancy. We did not see a significantly higher TFI prevalence among Black women with, compared to without, ectopic history, whereas we did among White women. Despite our relatively large sample of Black women, we may not have had enough Black women with ectopic pregnancy history to find a difference among Black women. It is possible that a known history of ectopic pregnancy may not be as common among Black compared with White women with TFI. Given higher STI rates among Black women,[9] it is also possible that these women had previous PID that was subclinical, which may lower awareness of a subsequent undiagnosed ectopic pregnancy if there was lower index of suspicion for pelvic pathology.

Although IVF data were missing for about 40% of women, one quarter of women with available data initiated IVF. Despite a similar proportion of Black and White women being offered IVF, the proportion of women with TFI who started IVF was nearly 5 times higher among White than Black women (PR, 0.2; 95% CI, 0–1.0). Although the proportion of women with IVF coverage was low for Black and White women, IVF coverage was lower for Black women. A prior study found that despite a lack of difference in the proportion of Black women accessing infertility care compared with the proportion of Black women in the general population, Black women were more educationally and economically disadvantaged compared with White women.[7] A nationally representative survey of women accessing medical care for infertility did not calculate estimates for Black women accessing ART because of the small number of Black women in the survey; however, based on the numbers required to report the data, it suggested that Black women accessed ART at least 10 times less often than White women.[12] Another national ART surveillance system reported the percent of White women undergoing IVF cycles was 10-fold higher than the percent of Black women.[20] In a study with the unique feature of equally covered IVF services, there was similar IVF utilization for Black and White women,[15] suggesting that lack of insurance coverage or health care access may be an issue in studies where access disparities exist, although another analysis noted persistent disparities in ART utilization by race comparing states with and without mandated IVF coverage.[14]

Although IVF initiation data were not complete, the available data from this study suggest lower proportions of intrauterine pregnancies and live births among Black women than White women with TFI, but we did not observe statistical differences for these outcomes.

Published studies have found somewhat conflicting results on IVF outcomes. In a group of women with equal health care coverage for IVF services, Black and White women had similar IVF pregnancy and live birth rates, although spontaneous abortion rates were higher in Black women.[15] Among women in a retrospective cohort study of IVF outcomes, the live birth rate was similar among Black and White women,[8] yet an older study of women presenting to an IVF practice found lower implantation rates and pregnancy rates in Black women.[19]

In our analysis, we found a higher TFI prevalence for Black compared with White women. Although clinic location and health insurance status may influence TFI prevalence among women, we found that observed TFI differences by these variables no longer persisted when stratified by race. Although race should be used to describe underlying biologic susceptibility to an outcome, such as TFI in this case, race often serves as a construct, or proxy for other factors such as socioeconomic status.[23] It is possible that observed differences in TFI prevalence by race may reflect differences in structural determinants of health among women. A larger prospective study of women with infertility with sufficient sample size, dedicated evaluation for confounders, and a multivariable adjustment for possible confounders would help to understand any independent contribution of race and structural health determinants to TFI. Other studies have assessed TFI severity,[24] yet we are unaware of studies that assessed racial disparities in TFI severity. Using our measure of severe disease, Black women had a nearly 3-fold higher prevalence of severe TFI than White women. This finding reinforces the importance of disparities in TFI. Although we had small sample sizes for women starting IVF and did not find statistically significant differences, potential reasons for possible disparities in IVF use include differences in insurance coverage, education, or income.

A strength of our analysis is that we assessed a random sample of all women seeking care for infertility within these clinics during the study period rather than limiting our analysis to women starting IVF. Our sample of women with TFI should thus be representative of women who sought care in these clinics during the study period. We also found racial disparities in TFI based on grade of TFI severity which reinforces our findings.

Additional limitations of our analysis include that these data were collected in 2011 to 2012, and our data are not generalizable to women who did not seek infertility care, such as those who lack health care insurance and/or access to such care. In addition, Black women may have been underrepresented in our sample. In the 2011 census data, the percentage of women that were Black was 33.6% in Birmingham (among Black and White women), whereas this percentage was 10.2% in Pittsburgh.[25] In our study, however, the percentage of Black women was only 21.2% in Birmingham and 12.6% in Pittsburgh. Despite being adequately powered to address our first objective, we had missing IVF initiation data for 55% of women with TFI. Differences in IVF initiation data by clinic and race could result in IVF initiation data not being representative of the clinic population. We also had small sample sizes of women initiating IVF with low precision and instability (demonstrated by wide CIs) for several estimates. This likely underpowered our ability to find differences in IVF treatment. Because data were extracted by different data abstractors at each site and we did not assess interrater reliability, there may be additional variability in the assessment of

documentation of offering IVF. Our data are also limited by the extent to which outcomes were documented in the records and we only documented outcomes by 2 years of follow-up. We also used a convenience sample of clinics which was not a random sample, thus our results are not generalizable beyond these 2 clinics.

Our data suggest racial disparities in TFI prevalence and possibly in treatment outcomes. Tubal factor infertility prevention can be advanced by recommended chlamydia and gonorrhea screening of sexually active women 24 years or younger.[26] From a public health standpoint, we should be aware of the need to prevent adverse reproductive outcomes in all women with a focus on those who bear the highest burden of these outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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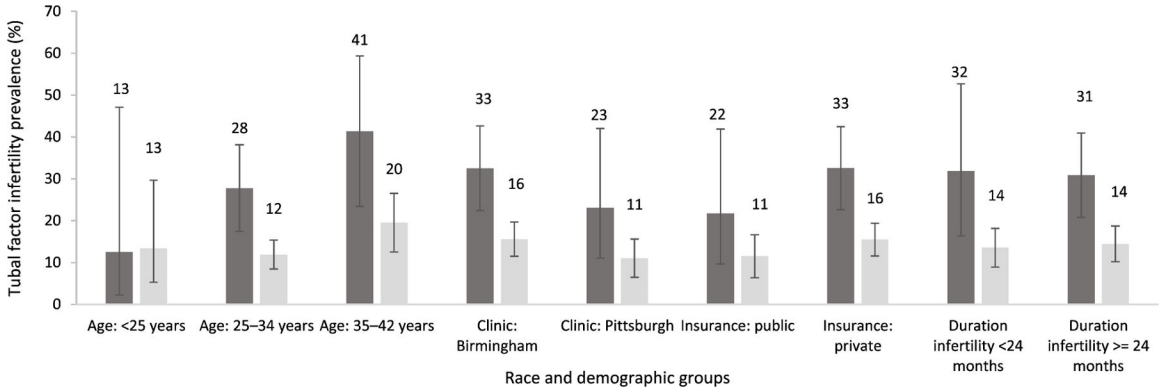

Figure 1.

Tubal factor infertility prevalence by race and other demographic characteristics for women of Black or White race, N = 598 women. Legend: Black (dark gray), White (light gray). Note: Wilson CIs are calculated for (1) Black women with: age less than 25 years, in the Pittsburgh clinic, with public insurance, and with duration of infertility less than 24 months; and (2) White women with: age less than 25 years.

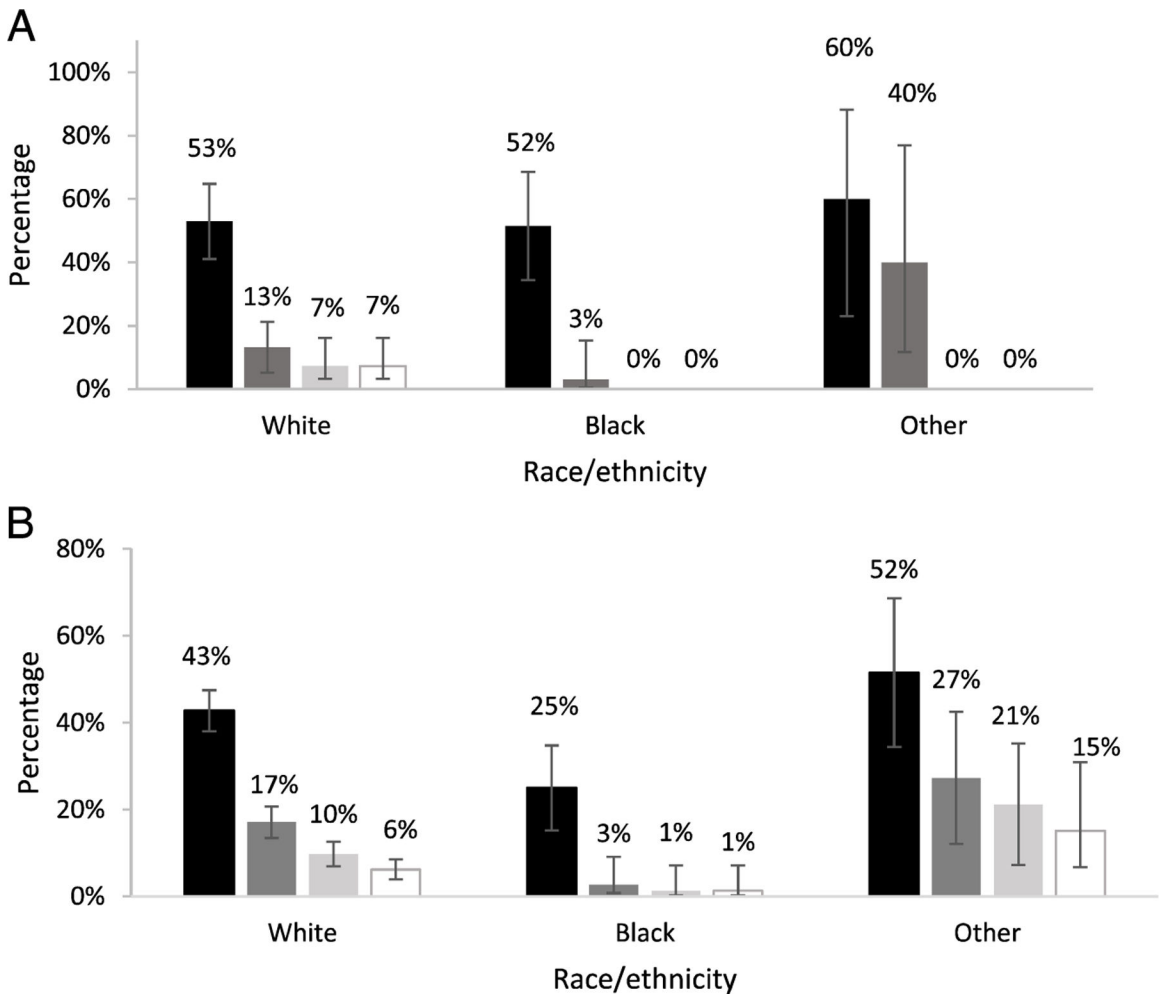

Figure 2.

A, In vitro fertilization (IVF) outcomes for tubal factor infertility (TFI) by race, n = 106 women, and (B) IVF outcomes for non-tubal factor infertility by race, n = 530 women. Legend: Offered IVF (black), IVF started (dark gray), intrauterine pregnancy (light gray), IVF live birth (white). Note: Percentages are calculated for women with outcome data among all women with infertility in the racial group. Wilson confidence intervals (CI) calculated for: (1) White women with TFI, with intrauterine pregnancy or live birth; (2) Black women with TFI, with IVF; (3) other women with TFI, with IVF offered, or IVF; (4) Black women without TFI, with IVF, or intrauterine pregnancy, or live birth; and (5) other women without TFI, with live birth.

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TABLE 1.

Prevalence of Tubal Factor Infertility by Various Patient Characteristics, N = 660 Women

Characteristics	Category	Total Characteristic N	Category n (%)	Tubal Factor Infertility Prevalence, % (95% CI)	PR for Tubal Factor Infertility (95% CI)
Overall		660		16.7 (13.8–19.5)	
Age group at new patient visit, y	<25	660	42 (6.4%)	11.9 (5.2–25.0) *	Reference
	25–34		449 (68.0%)	15.4 (12.0–18.7)	1.3 (0.6–3.5) *
	≥ 35		169 (25.6%)	21.3 (15.1–27.5)	1.8 (0.8–5.0) *
Race/ethnicity	White	636	489 (76.9%)	13.9 (10.8–17.0)	Reference
	Black		109 (17.1%)	30.3 (21.6–38.9)	**2.2 (1.5–3.1)** †
	Other		38 (6.0%)	13.2 (5.8–27.3) *	1.0 (0.3–2.0) *
Clinic location	Birmingham	660	409 (62.0%)	19.6 (15.7–23.4)	Reference
	Pittsburgh		251 (38.0%)	12.0 (7.9–16.0)	**0.6 (0.4–0.9)**
Health insurance coverage	Public	648	207 (31.9%)	12.6 (8.0–17.1)	Reference
	Private		441 (68.1%)	19.0 (15.4–22.7)	**1.5 (1.0–2.3)**
Health insurance coverage for IVF	No	645	546 (84.7%)	17.6 (14.4–20.8)	Reference
	Yes		99 (15.3%)	13.1 (6.5–19.8)	0.8 (0.4–1.3)
Ever pregnant ‡	No	660	354 (53.6%)	14.7 (11.0–18.4)	Reference
	Yes		306 (46.4%)	19.0 (14.6–23.4)	1.3 (0.9–1.8)
Prior spontaneous pregnancy	No	281	9 (3.2%)	0	Reference
	Yes		272 (96.8%)	19.9 (15.1–24.6)	Undefined
Prior ectopic pregnancy	No	284	253 (89.1%)	17.0 (12.3–21.7)	Reference
	Yes		31 (10.9%)	45.2 (27.5–62.8)	**2.7 (1.7–4.3)**
Prior IVF treatment	No	660	634 (96.1%)	16.9 (14.0–19.8)	Reference
	Yes		26 (3.9%)	11.5 (4.0–29.0) *	0.7 (0.2–1.7) *

* Wilson and likelihood ratio method used for CI.

† Significant CIs are indicated in bold.

‡ Indentation indicates characteristic is a subset of the overall category.

y, years; CI, confidence interval; IVF, in vitro fertilization; PR, prevalence ratio.

TABLE 2.

Prevalence of Starting IVF for Women With Tubal Factor Infertility, N = 50 Women

Characteristics	Category	Total Characteristics N	Category n (%)	Prevalence (%) of Starting IVF (95% CI)	PR for IVF (95% CI)
Overall		50		26.0 (13.4–38.6)	
Age group at new patient visit, y	<25	50	2 (4.0%)	0	Reference
	25–34		35 (70.0%)	34.3 (18.0–50.6)	Undefined
	≥ 35		13 (26.0%)	7.7 (1.4–33.3)*	Undefined
Race/ethnicity	White	48	29 (60.4%)	31.0 (13.6–48.5)	Reference
	Black		15 (31.3%)	6.7 (1.2–29.8)*	0.2 (0.0–1.0)*
	Other		4 (8.3%)	50.0 (15.0–85.0)*	1.6 (0.3–4.1)*
Clinic location	Birmingham	50	21 (42.0%)	23.8 (10.6–45.1)*	Reference
	Pittsburgh		29 (58.0%)	27.6 (10.7–44.4)	1.2 (0.4–3.4)*
Health insurance coverage	Public	50	25 (50.0%)	32.0 (13.1–50.9)	Reference
	Private		25 (50.0%)	20.0 (8.9–39.1)*	0.6 (0.2–1.6)*
Health insurance coverage for IVF	No	50	37 (74.0%)	24.3 (10.0–38.6)	Reference
	Yes		13 (26.0%)	30.8 (12.7–57.6)*	1.3 (0.4–3.2)*
Ever pregnant†	No	50	27 (54.0%)	22.2 (10.6–40.8)*	Reference
	Yes		23 (46.0%)	30.4 (15.6–50.9)*	1.4 (0.5–3.7)*
Prior spontaneous pregnancy	No	20	0 (0.0%)	N/A	Reference
	Yes		20 (100.0%)	25.0 (11.2–46.9)*	N/A
Prior ectopic pregnancy	No	23	17 (73.9%)	17.6 (6.2–41.0)*	Reference
	Yes		6 (26.1%)	66.7 (30.0–90.3)*	**3.8 (1.2–15.2)***,‡
Tubal surgery (remedial or otherwise)	No	50	41 (82.0%)	24.4 (10.8–38.0)	Reference
	Yes		9 (18.0%)	33.3 (12.1–64.6)*	1.4 (0.4–3.5)*
Prior IVF treatment	No	50	50 (100.0%)	26.0 (13.4–38.6)	Reference
	Yes		0 (0.0%)	N/A	N/A

*Wilson and likelihood ratio method used for CI.

†Indentation indicates characteristic is a subset of the overall category.

‡Significant CIs are indicated in bold.

N/A, not applicable; CI, confidence interval; IVF, in vitro fertilization; PR, prevalence ratio.