Infertility and treatment seeking practices among females and males with sickle cell disease in the SCDIC registry

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Abstract

Objective: To describe the prevalence of infertility and infertility treatment-seeking among people enrolled in the Sickle Cell Disease Implementation Consortium (SCDIC) registry and identify sociodemographic and clinical correlates of infertility.

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Design: Cross-sectional.

Participants: The study population included 2108 women and men (18 years of age) enrolled in the SCDIC registry who completed the fertility questionnaire.

Results: All participants who completed the infertility-specific questions were included in the analysis (1,224 females; 884 males). Of these, 16.9% of males and 23.7% of females reported infertility, in contrast to rates in the general population (12% of males; 11% of females). Only 22.8% of this subgroup had sought a fertility consultation; of these, 41% received infertility testing, and 58% received advice, yet only a few received specific treatment: ovulation medication (19.1%), fallopian tubal surgery (4.8%), other female treatment (17.5%), varicocelectomy (8.1%), or other male treatment (10.8%). Increasing age, employment status, and interaction between gender and single marital status are associated with reported infertility. We did not observe differences between groups relative to SCD genotype, a broad category of self-reported hydroxyurea use any time during life, type of medical insurance, income, or education.

Conclusion: To our knowledge, this is the first study to examine self-reported identification of and treatment for infertility among a large sample of people with sickle cell disease. These findings suggest that (a) infertility occurs at a higher rate but fertility care treatment-seeking is less frequent than in the general public; and (b) sociodemographic and clinical differences between individuals who report experiencing infertility and those who do not did not emerge in this study.

Introduction

Sickle cell disease (SCD) is an inherited hemoglobinopathy and one of the most common monogenetic disorders globally[1]. SCD is a multisystem disease characterized by sickle-shaped erythrocytes causing vaso-occlusive disease, vasculopathy, and systemic inflammation. Persons with SCD experience progressive multi-organ damage throughout their lifespan, starting in childhood[2]. Episodes of sickling are unpredictable and frequently occur, over time leading to hemolytic anemia, parenchymal injury, and eventually, chronic organ damage[3]. In the past, children with SCD died before reaching adulthood, but now, with the use of early interventions and close monitoring, they have a 98% overall survival rate to adulthood[4], resulting in increasing numbers of adults with SCD participating in family-planning decisions.

Both women and men can experience challenges to family building, including infertility, defined as the inability to achieve a clinical pregnancy following 12 months of regular, unprotected sexual intercourse[5]. Diminished ovarian reserve (DOR), in which there is a low oocyte supply, is a well-known risk factor for infertility[6]. Among females with SCD, data have identified an increased risk for diminished ovarian reserve compared to age-matched controls[7–9]. Specifically, Garba et al found that after controlling for age and body mass index, ovarian reserve as measured by serum Anti-Mullerian Hormone, was lower among those with HbSS versus HbAA[10]. Treatment for SCD may also impact fertility among women, with data to support that younger women ages 10 to 24 years of age treated

with hydroxyurea had higher rates of DOR[11]. Among males with SCD, evidence indicates that factors contributing to infertility include delayed puberty, low testosterone, and sperm abnormalities[12] due to testicular dysfunction[13]. Up to 24% of males with SCD develop hypogonadism, characterized by low testosterone production, infertility, erectile dysfunction, and poor libido[14]. Sickled erythrocytes can cause infarction and associated end-organ damage, such as testicular dysfunction and abnormalities in the accessory sex organs, including the seminal vesicles and the prostate gland, leading to significant decreases in ejaculate volume[15]. Approximately 40% of males with SCD suffer from painful priapism caused by the obstruction of venous outflow from the penis. Available studies suggest an association between hydroxyurea, a common and standard treatment for those with SCD, and reductions in overall sperm counts and motility, and increase in abnormal sperm morphology[16,17].

We are unaware of published reports regarding infertility prevalence and related treatment seeking among females and males with SCD. A fuller understanding of infertility and SCD in the United States may contribute to more patient-centered, robust fertility care for persons with SCD who seek genetic parenthood; therefore, to address this gap in the literature, we examined sociodemographic and treatment-seeking decisions related to infertility care among women and men living with SCD and currently enrolled in the Sickle Cell Disease Implementation Consortium (SCDIC) registry. The aims of this study were to (1) describe the prevalence of female and male factor infertility in persons with sickle cell disease in the SCDIC registry; 2) Describe infertility treatment seeking among females and males with infertility who are enrolled in the SCDIC registry; and 3) Determine if there are differences between the fertile and infertile group based on sociodemographic and clinical characteristics.

Materials and Methods

Design and Study Population

This study used a cross-sectional study design. The study population included all 2,440 women and men enrolled in the patient registry of the SCDIC, a consortium funded by the National Heart Lung and Blood Institute and comprised of eight comprehensive sickle cell disease centers and one data coordinating center in the United States. The consortium's primary goal is the improvement of care for people with SCD[18]; its recruitment strategy and data collection details can be found in previously published reports[18,19]. Recruitment for this study began in October 2017 with a minimum enrollment goal of 300 participants into the registry at each site (2,400 total) and occurred in outpatient clinics (e.g., sickle cell and primary care clinics), hospital inpatient settings, SCD support group meetings, conferences, and other platforms at the discretion of the centers and as their local IRB approval permitted.

Ethical Approval

Each of the eight SCDIC study sites sought local ethical approval prior to recruitment and data collection. Written informed consent was obtained before enrollment in the study. IRB approval was also obtained for this analysis of existing medical record data.

Data Collection and Measures

Consortium data were collected using self-report surveys, medical records, and laboratory abstraction forms. Full details regarding the data collection process and full content of patient surveys can be found in published reports[20]. Both female and male participants completed all data collection forms, which contained some infertility questions specific to the participant's biological sex. Of the 2,440 persons in the consortium, 2,374 completed pregnancy forms; of these, 2,315 responded to the infertility-specific questions (Figure 1). Women and men completed the infertility-specific surveys regardless of where they were in their family-building process. Infertility was defined as failure to conceive despite twelve or more months of regular unprotected intercourse, consistent with the World Health Organization and American Society of Reproductive Medicine definition of infertility[5]. Therefore, female participants were asked:

- Has there ever been a time in your life when you didn't become pregnant despite 12 or more months of regular unprotected intercourse?

- Did you ever go to a doctor or other medical care provider to talk about ways to help you have a baby?

- Which of the services did you have to help you have a baby? Check all the apply. (Advice; Infertility testing; Drugs to improve ovulation; Surgery to correct blocked tubes; Artificial insemination; Other types of medical help)

- Has a doctor or other medical care provider ever told you that you had fibroid tumors or myomas in your uterus?

- Has a doctor or other medical care provider ever told you that you had endometriosis?

Men were asked the following:

- Have you ever had a painful continuous erection, which is also called priapism?

- Has there ever been a time in your life during which you weren't able to get your partner pregnant despite 12 or more months of regular unprotected intercourse?

- Did you ever go to a doctor or other medical care provider to talk about ways to help you father a baby?

- Which of the following services did you have to help you father a baby? Check all that apply. (Advice; Infertility testing; Surgery to reverse a vasectomy; Treatment for varicocele; Other types of medical help)

- When you went for medical help to father a baby, were you ever told that you had any of the following male infertility problems? Check all that apply. (Sperm or semen problems; Varicocele; Other; None of the above)

In addition to collecting self-report demographic information, participants were also asked if they had 'ever' taken hydroxyurea, and if they were 'currently' taking hydroxyurea. Site research completed staff medical records, laboratory abstraction forms included SCD genotype and history of blood transfusions. Data for the medical and laboratory forms were abstracted from participants' electronic health records, entered into a REDCap database,

assessed for completeness and accuracy by the data coordinating center, and returned to each site for correction.

Data analysis

Baseline characteristics and distributions of risk factors were analyzed as frequencies and percentages for categorical variables and median and interquartile ranges (IQR) or mean and SD for continuous variables. Categorical variables were analyzed using chi-square or Fisher's exact test for sparse tables. Continuous variables were compared using t-test or Mann-Whitney U test, as appropriate. Two-sided p-values < .05 were considered statistically significant.

Modeling Strategy. The logistic regression model was developed in 2 phases. Initially, univariate analysis was used as a first screening step to analyze the association between infertility and sociodemographic and clinical variables hypothesized to be related to this outcome. These variables were selected based on subject matter expertise and prior scientific literature. Next, all variables considered to be biologically and socially influential factors were used in a multivariable regression model. These variables included age group (18–29, 30–34, 35+ years of age), gender, SCD genotype, history of hydroxyurea use (at any point in their lives), income, marital status, education, and employment status. Then, a backward elimination logistic regression with an exit criterion of p < .05 was used to identify statistically significant covariates and derive a more parsimonious final model. Interactions between selected predictors were included in the initial model, but the only significant interaction found was between gender and marital status. Model fitting also included a comparison of the full and reduced models to provide tests of improvement in fit assessed by the Schwarz Criterion and Akaike Information Criterion. Odds ratios (OR) and corresponding 95% confidence intervals were obtained for variables remaining in the final model. All analyses were conducted in SAS Version 9.4[21].

Results

The most up-to-date SCDIC Registry data were used to run these models, which included 2,440 SCDIC participants. We excluded participants <18 years of age to avoid confounding marital status, working status, and the highest level of educational attainment. This resulted in the total number of individuals (n = 2,108) included in this analysis (Figure 1).

Table 1 reports demographics, genotypes, and hydroxyurea use within the sample. Mean age was 29.2 years, and the majority were Black (95.6%) and never married (77.3%). Most participants (62.8%) reported Medicare/Medicaid/Military as their primary insurer. Most participants (73.4%) reported having the Hb SS genotype, and 73.8% reported taking or having taken hydroxyurea.

Of our study participants, 20.9% (n = 441; 23.9% of females and 16.9% of males), reported infertility, the reasons for which are provided in Figure 2. Only 22.8% (n = 100/441) of the participants who reported infertility had sought an infertility consultation; of these, 21.7% (n = 63) were female and 25% (n = 37) were male. Of the 100 participants who had sought a consultation, most had received advice (58% [n = 58 total]; 61.9% [n = 39] female; 51.4%

[n = 19] male); only 41% (n = 41) had received infertility testing (23.8% [n = 15] women; 70.3% [n = 26] males); and very few had received specific treatment: ovulation medication (19.1% [n = 12]), fallopian tubal surgery (4.8% [n = 3]), IUI (1.6% [n = 1], other female treatment (17.5% [n = 11]), surgery to repair a varicocele (8.1% [n = 3]), and other male treatment (10.8% [n = 4]).

In a comparison of those with infertility (n = 441) and without infertility (n = 1,667) (See Table 2), the multivariable model identified increasing age (p < 0.0001), employment status (p = 0.007), and interaction between gender and marital status (p = 0.01) as significantly associated with infertility. Compared to individuals 18–29 years of age, individuals 30–34 years of age had more than twice the odds (OR = 2.15, 95% CI [1.62–2.87])) of infertility, and those 35+ years had a 1.66 (95% CI [1.25–2.2) increase in odds for infertility. Unemployed individuals had higher odds of infertility (OR 1.31, 95% CI [1.03–1.67]) compared to those employed, while there was no statistically significant difference in the odds of infertility between the not employed by choice and the employed groups. Marital status was associated with infertility among males with males who had never been married having lower odds of reporting infertility compared to their married counterparts (OR = 0.36, .024–0.85, while for women, there was no statistically significant difference in the odds of infertility for those who were never married or were separated/divorces/widowed compared to their married counterparts (OR = 0.84, 95% CI [0.59–1.22] and OR = 1.38, CI (0.77–2.46, respectively). We did not observe differences between group with hydroxyurea use nor sickle cell genotype. In the full model including these 2 variables, odds ratios of infertility were not significantly different for patients with any history of hydroxyurea during lifetime (OR (95% CI)= 1.3 (0.9–1.7)), or for Hb SC or other genotypes compared with Hb SS (OR (95% CI)=0.9 (0.7–1.3) and OR (95% CI)= 1.4 (0.8–2.2), respectively.

Discussion

This study sought to increase understanding of infertility trends, treatment seeking, and possible sociodemographic and clinical characteristics in people with SCD and infertility challenges. The incidence of infertility reported by participants with SCD in our study (20.9% collectively, and by sex, 16.9% of males and 23.9% of females) was higher than national trends (about 12% of males and 11% of females)[22]. This is the largest cohort assessing infertility among men and women with SCD, and our findings about the incidence of infertility are consistent with other data, particularly concerning males with SCD[12]. Infertility in males with SCD has previously received more attention in the literature than infertility in females, which might be attributed to data suggesting that infertility among males with SCD has multiple causes, including hypogonadism, sperm abnormalities, and erectile dysfunction due to priapism[23]. However, there is recent attention on females with SCD and infertility. Evidence suggests that features specific to SCD, including chronic inflammation, oxidative stress, transfusion-related hemochromatosis, and ischemia injury to the ovaries increase the risk for inability to conceive[24]. Much of what is known about incidence of infertility has been derived from using the number of reported pregnancies during reproductive years as a surrogate for fertility. Studies comparing the pregnancy rates of people with and without SCD have surmised that women with SCD experience a lower number of pregnancies because fertility is reduced in women with SCD; however,

this is an imprecise approach[25]. A recent report examining reproductive outcomes of a large cohort of patients with SCD found that about a quarter of their adult female sample reported a pregnancy but much fewer among men[26]. It is important to note that this study did not examine intent for pregnancy or infertility was not collected, however the low rate of pregnancies is consistent with our findings. Premature ovarian insufficiency in women with SCD has historically been estimated by observational studies of the total rate of pregnancy, which is lower than that of the general population, but these data are insufficient as a basis for causal conclusions. In a previously report utilizing the same dataset as ours, hydroxyurea was found to be associated with miscarriage[26], however, it should be noted that repeat pregnancy loss (two or more miscarriages) denotes infertility, thus additional inquiry about pregnancy success over time for patients being treated with hydroxyurea is needed. Social influence on pregnancy seeking further complicates the use of pregnancy to infer fecundity. Research indicates that women with SCD are influenced by factors such as fear of pregnancy complications, increased pain during the pregnancy and birth, and overall lack of information from healthcare providers on reproductive planning[27].

Although our results demonstrated an increased risk of infertility with increasing age to the early thirties, the risk was not linear with the oldest age group. It is possible that individuals with infertility were underrepresented in the oldest age group. This may in part have been due to SCD treatment advances not being available to older women during their earlier reproductive years[28], hence not actively pursuing family building at the same rate as younger women. Also, this may be due to premature mortality in the population. A recent study by researchers from the Centers for Disease Control indicates that the median age at death of persons with SCD has increased from 28 years to 43 years[29]; however, a generally increased risk for infertility in persons with SCD remains[30].

In the US, about half of women between 15 and 44 years of age seek advice for infertility concerns[31]. In our study, only 22.5% of participants with infertility had sought an infertility consultation for advice, and 41% of these had received an infertility evaluation, a percentage significantly lower than in the general population. The American Society for Reproductive Medicine advocates for systematic and cost-effective infertility assessment for females[32] and accurate identification of male infertility and associated health conditions[33]. In most instances, private health insurance covers infertility evaluation, yet few states cover infertility diagnostic services (GA, HI, MA, MI, MN, NH, NM and NY) in at least one of their Medicaid plans (many of which limit coverage of infertility testing)[34,35]. Most likely, lack of coverage for infertility testing and treatment is a major barrier to patients with SCD; our findings have important policy implications for Medicaid plans nationally. It is important to note that only 26.5% of our participants had private insurance coverage; the majority (63.2%) reported Medicaid/Medicare as their insurance provider. Of the 100 participants in our study who reported infertility, very few had received medical help in conceiving. Most (58) had received advice, and ovulation medication was the treatment most often reported (n = 12). One participant reported having had intrauterine insemination, and none reported in-vitro fertilization (IVF). According to a recent Kaiser Family Foundation report, women from racial and ethnic minorities utilize infertility services less than non-Hispanic White women: only 13% of non-Hispanic White women and 7% of non-Hispanic Black women

nationally seek medical help to get pregnant[35]. While we recognize that SCD can affect people of all races, the majority in the U.S. are black, as reflected in our study's sample.

Given these challenges, comprehensively addressing inadequate access to care is essential. Although state efforts are slowly addressing access for the privately insured, legislative efforts on the federal level requiring private insurers to cover infertility services have made little forward progress. For example, the Access to Infertility Treatment and Care Act (HR 2803 and S 1461) would require the provision of infertility treatment by all health plans offered on group and individual markets (including Medicaid, EHBP, TRICARE, VA) but has never made it out of committee[35]. Additional efforts are needed to increase awareness about and access to fertility services for people with SCD. Most young adults with SCD have expressed a desire for future biological children, yet most receive little if any information about fertility from their healthcare provider[36]. In one study, less than half of the participants with SCD knew that SCD could have a negative impact on their future fertility[36]. Further, people with SCD and Medicaid may not realize that specific testing and treatments that impact fertility may exist for conditions related to their disease. However, their policy does not state this directly[35].

We examined whether there were differences based on sociodemographic and clinical characteristics between the fertile and infertile participants in our study and found that neither self reported hydroxyurea used ever during their lifetime nor sickle cell genotype were associated with infertility incidence. It is important to note that some current SCD treatments can have a significant impact on fertility status[37]. Patients with SCD who receive chronic transfusions often develop iron overload/buildup in the hypothalamus, pituitary, and ovaries[7]. Disruption of the hypothalamic-pituitary-gonadal axis in both sexes can cause hormonal changes leading to gonadal failure. Hydroxyurea, which is frequently used during the reproductive years, inhibits DNA synthesis in actively dividing cells, including gametes. Recent evidence found hydroxyurea is associated with diminished ovarian reserve[7,11,38]. A recent report of a small cohort of 33 young females with SCD on hydroxyurea looked at those who "ever took" hydroxyurea, and "currently exposed" to therapy, and found that 24% of participants had diminished ovarian reserve, suggesting hydroxyurea may be an infertility risk factor, however needs additional study. In males, the use of hydroxyurea has been associated with higher numbers of abnormal sperm, lower sperm count, and decreased fertility[39] with one study finding higher rates of oligospermia and azoospermia among men with SCD who are being treated with hydroxyurea[13]. Of note, there is some evidence of the protective nature of transfusions on sperm in the setting of pre-pubertal hydroxyurea use[7,40]. The meaning of our findings relative to hydroxyurea use is unclear given the variable used to measure hydrxyurea use was self reported use "ever during their lifetime". Some studies have associated the SCD genotype, specifically HbSS, with adverse birth outcomes[26,41]; however, to our knowledge, there are no other studies that have examined genotype differences in those with infertility. Our data did not uncover an association between infertility and genotype, however further verification is needed.

Fertility planning for people with SCD is very recently gaining attention and comprehensive recommendations for those seeking to build their families are available[42]. All women with

SCD would benefit from a consultation with a reproductive endocrinologist to discuss fertility preservation and surrogacy options[23,24].

Our study has several strengths, including a robust sample size sampled via a consortium with eight geographically diverse settings in the United States. This is the first large sample including data prospectively collected directly from men and women with questions about infertility and treatment seeking patterns. Women and men enrolled in the consortium continue to be followed through the prospective registry, allowing future inquiries to extend our study aims.

Limitations

Our study also has several limitations. First, as all participants with SCD were recruited from SCD specialty settings, findings may not be representative of people without access to SCD specialists; however, we believe our findings may overestimate treatment seeking because care providers in specialized centers typically refer women to gynecologists/reproductive endocrinologists, which is likely not the case for patients with SCD seen in non-specialty centers. Second, our results are not generalizable to patients with low English language literacy or who are non-English speaking. Third, infertility was self-reported. Although the definition of infertility was provided at the time of data collection, self-identification was not verified by a medical provider or laboratory markers of fertility potential (e.g., AMH and FSH for ovarian reserve and sperm count). These findings should be interpreted with caution because the mean age of participants was approximately 28 years, and the self-report infertility status, and participants who were fertile may not have tried to conceive at the time of the survey. It is important to note that our participants were asked about the inability to become pregnant after one year of unprotected intercourse, which is the definition of infertility for otherwise healthy people under 35 years of age, however, the time reduces to 6 months for those 35 years of age and older[5]. This was not reflected in our study and thus may have affected the results, and it should also be noted that we currently do not know the age threshold for infertility for people with SCD given the global acceleration of age. Importantly, there are limitations to the data related to HU use. The data was self reported use ever during their lifetime. We were unable to assess whether participants were actually ever taking HU on a consistent basis during the time of pregnancy or pregnancy attempts. Laboratory data verifying hydroxyurea use, and a control group, would be required to assess causality. Finally, this study is limited by its use of a cross-sectional design. The timing of participants' completion of the study surveys and the abstraction of their medical records may not fully reflect their experience of infertility during or later than their family-building phase.

Conclusion and Future Directions

To our knowledge, this is the first study to examine the prevalence of and treatment seeking for infertility among a large sample of women and men with SCD. These findings suggest that (a) infertility occurs at a higher rate in this population than in the general public, (b) infertility care treatment seeking in this population is less frequent than in the general public, and (c) only increased age and unemployment were associated with a higher likelihood of

reporting infertility; no clinical differences were observed. It is important to continue to pursue knowledge about infertility in populations of people with SCD and advocate for fair and equitable access to related testing and treatment, regardless of location, financial status, or insurance provider.

Funding statement:

Data Availability Statement:

We have ethical restrictions about openly releasing the data set to the public as the nature of the data set would result in loss of participant anonymity. The ethical restrictions were imposed by the Sickle Cell Disease Implementation Consortium (SCDIC). However, data set requests can be made to SCDIC and their data coordinating center at RTI international. Requests will be reviewed by the SCDIC Publications Committee. Data set requests can be sent to SCDIC at scdic-publications-subcommittee@rtiresearch.org or +1 301-230-4674.

Abbreviations key:

SCD	Sickle cell disease
SCDIC	Sickle Cell Disease Implementation Consortium
OR	Odds ratio
IVF	In-vitro fertilization

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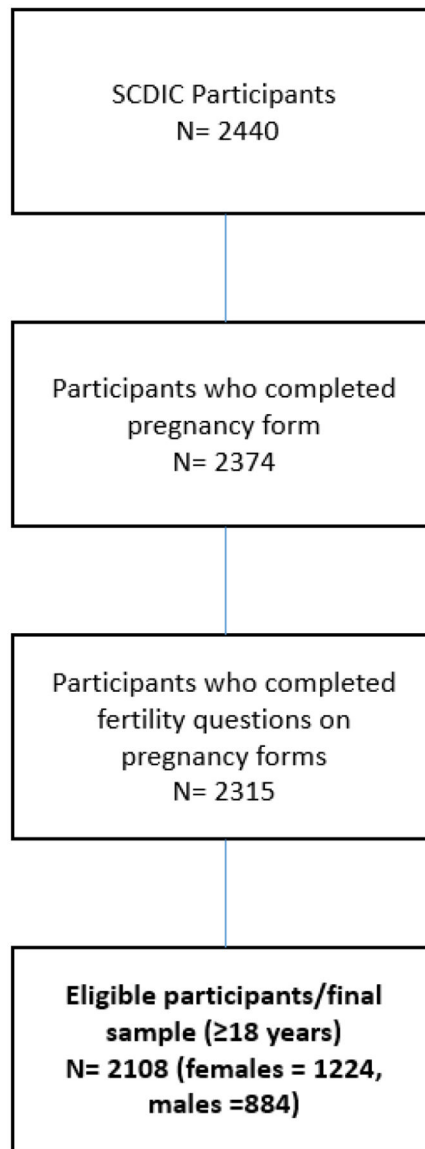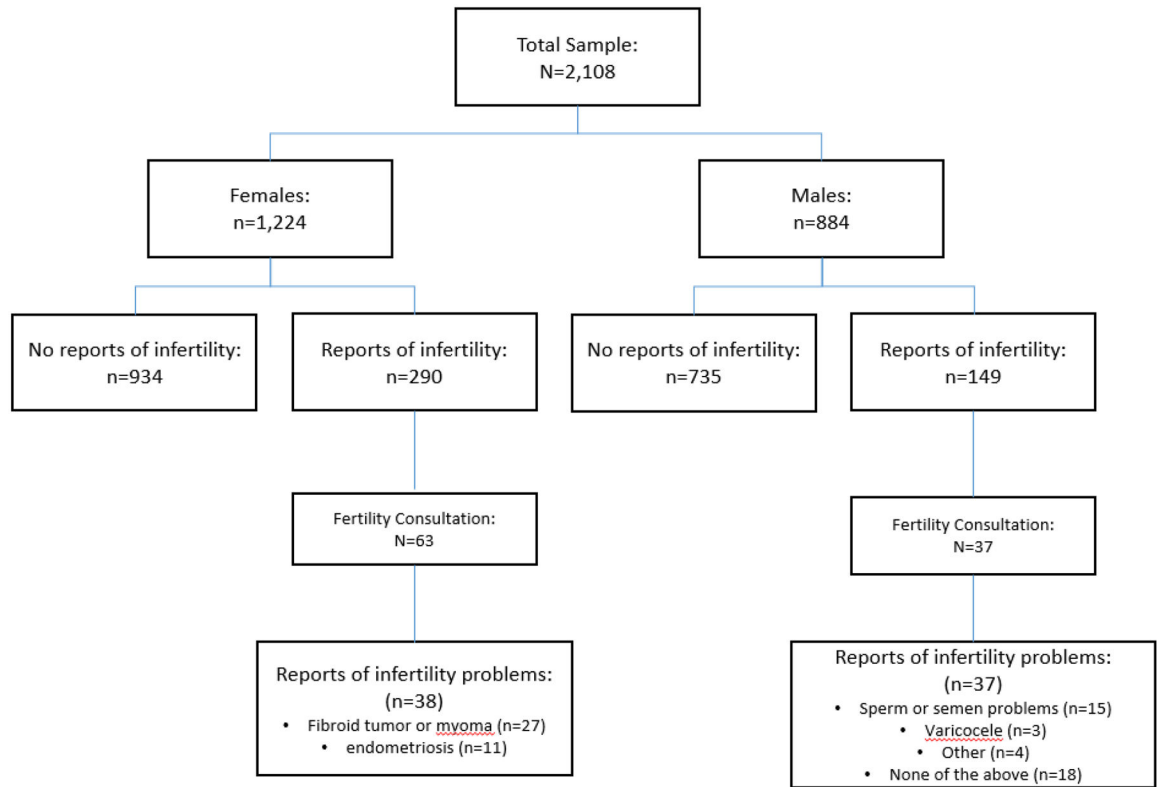
FIGURE 1.
Eligibility for final sample

FIGURE 2.
Prevalence & Diagnosis of Female & Male Factor Infertility

TABLE 1.

Sample Demographic and baseline characteristics by gender

Characteristic	Females (n = 1,224)	Males (n= 884)	Total (n = 2108)
Age at enrollment			
Mean (SD) years	29.4 (7.1)	28.9	29.2 (7.2)
Median (Q1–Q3)	29 (24–35)	28 (23–24)	28 (23–24)
Range (min-max)	(18–45)	(18–45)	(18–45)
Age groups, n, %			
18–29	665 (54.3%)	510 (57.7%)	1175 (55.7%)
30–34	243 (19.9%)	163 (18.4%)	406 (19.3%)
35+	316 (25.8%)	211 (23.9%)	527 (25.0%)
Race, n (%)			
American Indian/Alaska Native	7 (0.6%)	4 (0.5%)	11 (0.5%)
Asian	2 (0.2%)	2 (0.2%)	4 (0.2%)
Black	1148 (96.2%)	814 (94.8%)	1962 (95.6%)
Multi-racial	31 (2.6%)	35 (4.1%)	66 (3.2%)
White	5 (0.4%)	4 (0.5%)	9 (0.4%)
Missing (no response) [*]	31 (2.5%)	25 (2.8%)	56 (2.7%)
Ethnicity			
Hispanic/Latino	59 (5.0%)	46 (5.3%)	105 (5.1%)
Missing (no response) [*]	33 (2.7%)	13 (1.5%)	46 (2.2%)
Marital status			
1. Never married	905 (77.7%)	637 (76.7%)	1542 (77.3%)
2. Married/Living as married	184 (15.8%)	137 (16.5%)	321 (16.1%)
3. Divorced/separated/widowed	75 (6.4%)	56 (6.7%)	131 (6.6%)
Missing (no response) [*]	60 (4.9%)	54 (6.1%)	114 (5.4%)
Education			
Less than High School	12 (1.0%)	14 (1.6%)	26 (1.2%)
Some high school	93 (7.7%)	89 (10.2%)	182 (8.7%)
High school graduate or GED equivalent	306 (25.3%)	311 (35.6%)	617 (29.6%)
Some college or vocational training	440 (36.3%)	295 (33.8%)	735 (35.3%)
College graduate	360 (29.7%)	164 (18.8%)	524 (25.1%)
Missing (no response) [*]	13 (1.1%)	11 (1.2%)	24 (1.1%)
Employment			
Working now	466 (38.8%)	345 (40.1%)	811 (39.3%)
Not employed by choice	227 (18.9%)	138 (16.0%)	365 (17.7%)

Characteristic	Females (n = 1,224)	Males (n= 884)	Total (n = 2108)
Not employed, other	509 (42.3%)	378 (43.9%)	887 (43.0%)
Missing (no response) *	22 (1.8%)	23 (2.6%)	45 (2.1%)
Income			
$25,000 and under	626 (56.5%)	388 (50.8%)	1014 (54.2%)
$25,001 – $50,000	240 (21.7%)	180 (23.6%)	420 (22.4%)
$50,001 – $75,000	105 (9.5%)	100 (13.1%)	205 (11.0%)
$75,001 – $100,000	54 (4.9%)	47 (6.2%)	101 (5.4%)
>$100,000	82 (7.4%)	49 (6.4%)	131 (7.0%)
Missing (no response) *	117 (9.6%)	120 (13.6%)	237 (11.2%)
Medical Insurance			
None	143 (11.7%)	90 (10.2%)	233 (11.1%)
Medicare, Medicaid or military health plan	773 (63.3%)	548 (62.1%)	1321 (62.8%)
Private	305 (25.0%)	245 (27.7%)	550 (26.1%)
Missing (no response) *	3 (0.2%)	1 (0.1%)	4 (0.2%)
SCD genotype			
Hb SS or Hb B0	876 (72.3%)	660 (74.9%)	1536 (73.4%)
Hb SC disease	256 (21.1%)	178 (20.2%)	434 (20.7%)
Hb B+	67 (5.5%)	34 (3.9%)	101 (4.8%)
Other	13 (1.1%)	9 (1.0%)	22 (1.1%)
Missing *	12 (1.0%)	3 (0.3%)	15 (0.7%)
Hydroxyurea use, ever	874 (72.1%)	670 (76.2%)	1544 (73.8%)
Missing *	11 (0.9%)	5 (0.6%)	16 (0.8%)
Hydroxyurea use, current	526 (43.9%)	465 (53.3%)	991 (47.9%)
Missing *	25 (2.0%)	12 (1.4%)	37 (1.8%)
History of blood transfusions	976 (64.8%)	251 (64.7%)	1227 (64.7%)
Missing *	162 (9.7%)	51 (11.6%)	213 (10.1%)

Patients with missing data are not included in calculations of percentages unless otherwise specified

*
Number missing is included for informative purposes only, Percent of missing values computed as proportion of eligible population (n = 2,108)

TABLE 2.

Final multivariable logistic regression model for infertility

	Results of final multivariable logistic regression model for infertility	
Variables	**Overall type III p-value**	**OR (95% CI)**
Age	**< 0.0001**	
18–29		Ref
30–34		2.15 (1.62–2.87) [**]
35+		1.66 (1.25–2.2) [**]
Employment	**0.007**	
Working now		Ref
Not employed by choice		0.79 (0.54–1.12)
Not employed, other		1.31 (1.03–1.67) [*]
gender*marital status[§]	**0.01**	
Male		
Married/Living as married		Ref
Never married		**0.36 (0.24–0.58)** [**]
Divorced/separated/widowed		0.68 (0.33–1.34)
Female		
Married/Living as married		Ref
Never married		0.84 (0.59–1.22)
Divorced/separated/widowed		1.38 (0.77–2.46)
[*]Defined as a "yes" response to question "[has there] ever been a time in your life during which you didn't become pregnant/weren't able to get your partner pregnant despite 12 or more months of regular unprotected intercourse?"		

[**]
p .001,

[*]
p < 0.05

[§]Marital status and gender were added in the regression also as main effects. ORs are not reported separately for these variables as they depend on the level of the interacting variable