Sexual orientation of women does not affect outcome of fertility treatment with donated sperm

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Submitted on October 1, 2013; resubmitted on November 7, 2013; accepted on November 18, 2013

STUDY QUESTION: Is there a difference in fertility between heterosexual women and lesbians undergoing sperm donation?

SUMMARY ANSWER: Women undergoing treatment with donated sperm are equally fertile regardless of sexual orientation.

WHAT IS KNOWN ALREADY: Lesbians have an increased prevalence of smoking, obesity, sexually transmitted diseases and, possibly, polycystic ovary syndrome, all factors known to affect fertility. Previous studies on sperm donation inseminations (D-IUI) show conflicting results regarding pregnancy outcome.

STUDY DESIGN, SIZE, DURATION: This is a national study of 171 lesbians and 124 heterosexual women undergoing sperm donation both as D-IUI (lesbian n = 438, heterosexual n = 298) and as embryo transfers (ET) after IVF with donated sperm (lesbians n = 225, heterosexuals n = 230) during 2005–2010.

PARTICIPANTS/MATERIALS, SETTING, METHODS: All clinics in Sweden offering sperm donation recruited patients. Differences in patients’ medical history, treatment results and number of treatments to live birth were analyzed using independent samples t-test, Pearson’s χ² test or Fisher’s exact probability test.

MAIN RESULTS AND THE ROLE OF CHANCE: 71.8% of heterosexuals and 69.0% of lesbians had a child after treatment. The mean number of treatments was 4.2 for heterosexual women and 3.9 for lesbians. The total live birth rate, regardless of treatment type, was 19.7% for heterosexuals and 19.5% for lesbians. For D-IUI, the live birth rate was 12.8% for heterosexuals and 16.0% for lesbians and the live birth rate for all IVF embryo transfers (fresh and thawed cycles) was 28.7% for heterosexuals and 26.2% for lesbians. There were no differences in live birth rate between the groups for each of the different types of insemination stimulations (natural cycle; clomiphene citrate; FSH; clomiphene citrate and FSH combined). Nor was there a difference in live birth rate between the groups for either fresh or thawed embryo transfer. There was no difference between the proportions of women in either group or the number of treatments needed to achieve a live birth. Heterosexuals had a higher prevalence of smokers (9.2%), uterine polyps (7.2%) or previous children (11.3%) than lesbians (smokers 2.8%, P = 0.03; polyps 1.8%, P = 0.03; child 2.5%, P = 0.003).

LIMITATIONS, REASONS FOR CAUTION: This study is limited to women living in stable relationships undergoing treatment with donated sperm in a clinical setting and may not apply to single women or those undergoing home inseminations.

WIDER IMPLICATIONS OF THE FINDINGS: These results may influence healthcare policy decisions as well as increase the quality of clinical care and medical knowledge of healthcare professionals. The data also have important implications for individuals regarding screening, infertility diagnostic procedures and treatment types offered to heterosexuals and lesbians seeking pregnancy through sperm donation.

STUDY FUNDING/COMPETING INTEREST(S): Funding was granted by the Stiftelsen Familjeförening och Namninförening i Uppsala; the Swedish Research Council for Health, Working Life and Welfare; and the Marianne and Marcus Wallenberg Foundation. The authors report no conflicts of interest.

Key words: insemination / IVF / lesbian / pregnancy / sperm donation
Introduction

There are few studies regarding fertility differences between heterosexuals and lesbians (NIH, 2011) and often the results are conflicting. It is estimated that 2–12% of the female population is lesbian (Markus et al., 2010). Many lesbians do not inform their physicians of their sexual orientation and often the physician assumes they are heterosexual (McNair and Hegarty, 2010). The literature on childbirthing lesbians is limited, mostly pertaining to psychosocial aspects or parenting abilities. Several investigations have identified gaps in the medical professions knowledge regarding this population (Denenberg, 1995; Abdessamad et al., 2013). Few studies have examined the medical conditions of women receiving sperm donation and only a handful compare heterosexuals and lesbians (Ferrara et al., 2000; De Sutter et al., 2008; Linara et al., 2011).

Fertility outcomes could be different in lesbians compared with heterosexual women because of difference in lifestyle factors and the incidence of gynecological conditions. An increased incidence of smoking (Balsam et al., 2012; Kabir et al., 2013); obesity (Boehmer and Bowen, 2009; Fogel et al., 2012); and risk for/prevalence of sexually transmitted diseases (STDs; Lemp et al., 1995; Singh et al., 2011; Marrazzo and Gorgos, 2012) have been reported. One study has found an increased prevalence of polycystic ovary syndrome (PCOS) in lesbians (Agrawal et al., 2004). Brodin et al. (2013) have shown that women with PCO ovaries have an increased chance of pregnancy when undergoing IVF treatment. This might indicate that lesbians would have a higher chance of pregnancy when undergoing IVF. No difference in prevalence of menstrual dysfunction or endometriosis based on sexual orientation has been found (Johnson et al., 1987).

Whereas home insemination is not regulated, Swedish law has allowed for intrauterine insemination with donated sperm (D-IUI) at fertility clinics for heterosexual couples for decades and IVF with donated sperm (D-IVF) has been allowed since 2003. Female lesbian couples have been allowed treatment with donated sperm since 2005 (Law 2009:262, 2005:445). Sperm donation treatment for lesbian couples is usually based on social rather than medical indications. Gamete donation is only allowed at university clinics in Sweden. Only couples living in a stable relationship are allowed to undergo sperm donation after going through a screening process with a counselor and physician. The allowed number of publically financed treatments varies between local healthcare authorities. Also, the eligibility criteria differs to some extent between clinics, for example, the upper age limit for treatment for women is often 38–40 years and the upper BMI limit is 30–35 kg/m². Only couples without severe physical or mental illnesses are allowed treatment and those who do not have a child together are covered by the public healthcare system.

The aim of this study is to determine if there is a difference in fertility between heterosexuals and lesbians undergoing sperm donation treatment. To achieve the aim of this study, the following specific research questions are posed:

(i) Is there a difference in demographic factors affecting fertility between heterosexuals and lesbians undergoing sperm donation treatment?
(ii) Is there a difference in pregnancy outcome between heterosexuals and lesbians undergoing sperm donation treatment?
(iii) Is there a difference in number of treatments to live birth between heterosexuals and lesbians undergoing sperm donation treatment?

Materials and Methods

Heterosexual and lesbian couples undergoing sperm donation treatment were recruited between the years 2005 and 2008 in this national study. Treatment data are included from the first sperm donation treatment until 31 December 2010. All Swedish clinics offering sperm donation treatment have participated. All couples undergoing treatment with sperm donation were approached for study participation. Heterosexual (n = 158) and lesbian couples (n = 197) were given oral and written study information. All participants signed an informed consent. Of those included, 124 (78.5%) were heterosexual couples and 168 (85.3%) were lesbian couples (Fig. 1). Reasons for non-participation or non-inclusion were: did not want to participate, no treatment given, not understanding Swedish or unknown.

Only women completing at least one treatment with donated sperm were included. Treatment cycles for siblings were also included. By reviewing medical records of all couples, background factors that could affect fertility have been examined as well as data regarding treatment and results.

Study population

Background and treatment information has been received regarding 124 heterosexual couples and 168 lesbian couples. Two lesbian couples, who had a child after treatment, were allowed to switch the partner receiving treatment so that the non-biological mother was given treatment for a sibling. One lesbian couple switched treatment partner after two failed IVFs, as the first partner produced few oocytes despite high-dose follicle-stimulating hormone (FSH). Thus, 168 lesbian couples have participated and 171 lesbians have received treatment. Most clinics, at the time of the study, only allowed for treatment of one partner ever, even if the couple wished to switch for a following treatment or for sibling treatment. There was no difference in the number of couples who underwent sibling treatment [heterosexuals n = 25 (20.2%); lesbian n = 24 (14.0%), P = 0.16].

Statistical analysis

All statistical analysis was performed using the Statistical Package for the Social Sciences 21.0 for Windows software package. To compare differences in mean values, an independent samples t-test was used. Bivariante differences in categorical data were analyzed using a Pearson’s χ² test or, if applicable, a Fisher’s exact probability test. All statistical tests were two-sided, P-values of <0.05 were considered to be statistically significant.

Ethical approval

This study was approved by the Regional Ethical Review Board in Linköping (Dnr M129-05-050223, T113-07 080122).

Results

Demographic factors

Demographics of the study population are displayed in Table I and Supplementary data, Table S1. The proportion of smokers was statistically higher among treated heterosexual women (9.2%) than lesbians (2.8%). Previous gynecological problems were at least twice as common among lesbians for the following diagnoses: chlamydia, salpingitis, endometriosis, operation for ovarian cyst and uterine fibroids although none of these differences were statistically significant. There was no difference between the number of women with patent Fallopian tubes for the total group [heterosexuals n = 85/96 (88.5%), lesbian n = 113/132 (85.6%), P = 0.73] or for the women undergoing D-IUI [heterosexuals n = 80/81 (98.8%), lesbian n = 111/116 (95.7%), P = 0.46]. More heterosexual women...
(7.2%) than lesbians (1.8%) had undergone hysteroscopy for uterine polyps.

**Previous treatment**

Regarding previous treatment, lesbians (60.3%) had previously undergone D-IUI more often than heterosexual women (22.9%, \( P < 0.001 \)). Heterosexual women (26.3%) had previously undergone IVF with intracytoplasmic sperm injection (ICSI) treatment with partner sperm whereas none of the lesbians had undergone ICSI treatment within a previous heterosexual relationship. The heterosexual couples who had previously undergone ICSI had extremely poor sperm quality and the chance of pregnancy was deemed futile so treatment was switched to sperm donation. Although the proportion of women who had undergone D-IVF was more than twice as high for lesbians, there was no statistical difference (\( P = 0.42 \)).

**Previous pregnancies**

Both heterosexuals and lesbians who underwent treatment had previous pregnancies before participation in this study (see Table I). There was no difference in the total number of pregnancies, the proportion of those who had a legal abortion, a miscarriage or an extra-uterine pregnancy. The number who had a child previously was higher among heterosexual women (11.3%) than treated lesbians (2.5%). Both heterosexuals and treated lesbians had previous pregnancies within their current relationship (Supplementary data, Table SI).

**Treatments given**

A total of 1191 treatments were given: 528 to heterosexuals and 663 to lesbians (Fig. 2). The mean number of treatments per couple was 4.2 for heterosexuals and 3.9 for lesbians. Lesbians underwent more D-IUI treatment cycles than heterosexual women, who underwent D-IVF more often. Within the group who underwent D-IVF, more lesbians had previous failed D-IUI [heterosexuals \( n = 12/49 \) (24.5%), lesbians \( n = 33/43 \) (76.7%), \( P < 0.0001 \)] whereas more heterosexual women had undergone a failed ICSI treatment [heterosexuals \( n = 11/49 \) (22.4%), lesbians \( n = 0/42 \), \( P = 0.001 \)].

**Pregnancy outcome**

In this study, 89 (71.8%) heterosexual couples and 116 (69.0%) \( P = 0.25 \) lesbian couples had at least one child after treatment. There was no difference in the pregnancy rate, overall live birth rate, singleton births, twin births or miscarriages for either group (Fig. 2) disregarding treatment type.

When examining the overall number of pregnancies with D-IUI regardless of stimulation type [natural cycle (NC); clomiphene citrate; FSH; combination clomiphene citrate and FSH cycle (clomiphene citrate/FSH)], more lesbians became pregnant (20.5%) than heterosexual women (14.8%) although there was no difference in live birth rate. Pregnancy, miscarriage and live birth rates for each group within each treatment type [NC, clomiphene citrate, FSH or clomiphene citrate/FSH cycle D-IVF, FET or embryo transfer fresh and thawed (ET)] did not differ (Fig. 2).

**Number of treatments to first live birth**

It was not possible to examine the number of treatments needed to achieve a first pregnancy so live birth was studied. The number of treatments needed to achieve a first live birth was studied for (i) those undergoing D-IUI, (ii) those undergoing D-IUI exclusively, (iii) those undergoing ET (iv) those undergoing ET exclusively and (v) those undergoing treatment regardless of type. A subgroup analysis was also carried out for those with no previous D-IUI.

There was no difference between the groups in the proportion of women achieving a live birth when analysing subgroups undergoing the above mentioned treatment types (Fig. 3). Since having a failed D-IUI before entering this study might imply a lower fertility, a subgroup analysis was performed on those who had never undergone D-IUI. For these
women, the mean ± SD number of total treatments to first live birth did not differ between groups for (i) those undergoing D-IUI exclusively (heterosexuals 1.8 ± 1.3, lesbians 1.9 ± 1.8, \(P = 0.83\)), (ii) those undergoing D-IVF exclusively (heterosexuals 1.6 ± 1.1, lesbians 3.0 ± 1.4, \(P = 0.17\)) or (iii) for all treatments (heterosexuals 1.8 ± 1.5, lesbians 1.7 ± 1.7, \(P = 0.80\)).

**Discussion**

The results of this study show few differences in background factors that would indicate a difference in fertility based on sexual orientation. Live birth rate and number of treatments to first live birth did not differ between groups even when comparing groups within different treatment type.

A larger number of lesbians were given treatment. This may reflect the change in the law which occurred at the start of the study. However, future studies may find more lesbians seeking D-IUI than heterosexual couples. Azospermic or other causes where heterosexual couples need D-IUI are relatively uncommon in comparison with lesbians who have a social cause. Clinical D-IUI as opposed to home inseminations may be preferred by lesbians due to legal issues or other reasons (Nordqvist, 2011).
Regarding background factors that might affect fertility, differences were found in the prevalence of smokers, polyps, prior treatments and those with previous children. Fewer lesbians than heterosexuals in this study smoked, which should imply a higher fertility. Contrary to the results in this study, there are several studies reporting increased tobacco usage in lesbians compared with heterosexual women (Balsam et al., 2012; Kabir et al., 2013). However, the studies often recruit participants through sexual minority organizations and these studies also reflect a larger population, not just those wanting to conceive. Furthermore, it has been reported that lesbians may fear discrimination based on healthcare providers’ attitudes or in the treatment given (Durso and Meyer, 2013). In this study, there may be a reporting bias among lesbians as smoking is taboo in pregnancy within the Swedish culture and lesbians may have unnecessarily feared refusal of treatment. Similar to the findings in this study, Moegelin et al. (2010) published the first study in Sweden comparing the gynecological health of women attending (i) a special clinic for women who have sex with women (WSW) and (ii) women attending the regular clinic. They found a lower frequency of smoking among women attending the clinic for WSW. This may imply that there may be a difference in smoking discrimination.
among lesbians in Sweden due to cultural differences. Smoking adversely affects the reproductive outcome by several mechanisms including the impact on ovarian reserve, which can be indirectly assessed using basal FSH (Caserta et al., 2013). However, there was no difference in mean basal FSH between the groups, indicating that ovarian reserve is probably equal between the groups.

Pertaining to previous gynecological problems known to lower fertility, the prevalence of chlamydia, salpingitis, endometriosis, operation for ovarian cyst and fibroids was higher among the treated lesbians although there was no statistical difference. The prevalence of chlamydia has been reported as higher among lesbians (Lemp et al., 1995; Marrazzo and Gorgos, 2012) but in the Swedish study by Moegelin et al. (2010), there was a lower frequency of patient-reported history of chlamydia among WSW women. Also, in the Moegelin study, it was noted that many of the women attending the WSW clinic had not previously undergone a gynecological exam within 5 years and it is therefore uncertain if the WSW had an actual lower rate of STDs or if the lower rate was due to nondiagnosis. Despite the higher prevalence of chlamydia, no difference in tubal patency was found. This result is similar to other studies of women undergoing insemination that also found no difference in tubal patency between lesbian and heterosexual women (Ferrara et al., 2000; Agrawal et al., 2004).

In contrast to the study by Agrawal et al. (2004) where an increased prevalence of PCOS was found in lesbians seeking ovulation treatment with or without insemination, there was no difference in the prevalence of PCOS or proportion of women with irregular menstrual periods in our study. There are several other studies which also could not find a difference in PCOS prevalence based on sexual orientation (De Sutter et al., 2008; Smith et al., 2011).

Another gynecological problem that lowers fertility is uterine polyps and, in this study, more heterosexual women had undergone hysteroscopy for polyp extraction. This is the first reported difference and might reflect screening differences between the groups. An alternative reason may be the fact that more heterosexual women had previously undergone ICSI, implying that these women may have undergone more ultrason examinations, thus increasing the chance of discovery of polyps.

Having undergone previously failed D-IUI could mean a lower fertility. More lesbians had undergone failed D-IUI prior to being included in the study, which reflects the change in the law. Before Swedish law allowed for treatment of lesbians, many lesbians chose to seek treatment outside the country or to do home inseminations. Only heterosexual women had a failed ICSI treatment with partner sperm previously, which is to be expected as it is common practice to use ICSI, if at all possible, as a method of choice over sperm donation.

The number of prior pregnancies among women within a group might be an indication of increased fertility. Alternatively, the difference may be due to dissimilarities in lifestyle factors, such as contraceptive usage or the number of pregnancy opportunities, and, thus, not be due to a difference in fertility. Interestingly, both groups had pregnancies previously, both within previous relationships and even within the same relationship. More heterosexual women were biological mothers, both in previous relationships and within the same relationship, than lesbians. However, regarding the number of legal abortions, miscarriages and extra-uterine pregnancies there was no difference based on sexual orientation. There are reports of increased numbers of teenage or early adulthood pregnancies among lesbians (Saewyc et al., 2008) which might explain the same
Strengths and limitations
This is the first national study investigating if there is a difference in fertility based on sexual orientation for women who underwent sperm donation. Also, it is the first study examining treatment results stratified by treatment type and sexual orientation and also the first examining the results of D-IVF based on sexual orientation. Number of treatments to first live birth is also examined for the first time.

As this is a national study, there are a large number of women included and individual differences between clinics are reduced. A strength of this study is that the women are living in a stable heterosexual or lesbian relationship. However, it has not been studied whether the women are exclusively heterosexual or lesbian. Nor does it examine the non-treated lesbian partner’s fertility or single women’s fertility. Many lesbians do home inseminations with donated sperm (Nordqvist, 2011) and, due to the timing of this study and the change in the law, these women may not be included in this study if they have had a child. This study started from the time lesbians were first legally allowed treatment within Sweden, which may mean that the average age for lesbians seeking sperm donation currently may be lower than in this study. The time difference for legally allowed treatment between treatment groups may mean that the study population of lesbians represents a lower socioeconomic group, as those with higher education levels or better personal finances may have been able to afford treatment outside the country before being permitted to do treatment within Sweden. However, women in lower social economic groups or lower education levels are known to smoke more often and have a higher BMI (Connor et al., 2013). Since there was a lower prevalence in smoking among lesbians and no difference in BMI or relationship length between groups, it can be interpreted to mean that there is no large socioeconomic difference between the groups.

This study has avoided recall bias through the examination of medical records. However, the background data have been dependent on the detail of the examining physician’s clinical notes. A limitation in the study is that women were allowed differing number of treatments due to differing healthcare coverage or the individual clinic’s eligibility criteria. However, the differences between the groups were the same because each clinic recruited approximately the same number of heterosexuals as lesbian couples.

Clinical significance and future studies
Research in this area is important as it may influence healthcare policy decisions as well as increase the quality of clinical care and medical knowledge of healthcare professionals. It also has important implications for individuals regarding screening, infertility diagnostic procedures and treatment types offered to heterosexuals and lesbians seeking pregnancy through sperm donation. There is a limited amount of research pertaining to lesbians wishing to conceive. Healthcare professionals have a limited knowledge about this population and also express a desire for more information (Abdessamad et al., 2013). This study shows the importance of good screening procedures in order to facilitate choice of the best treatment for each individual. We have only studied women living in stable heterosexual and lesbian relationships and future studies are needed regarding single women based on sexual orientation. The decision process the lesbian couple goes through as to which partner will receive treatment needs to be examined.

In conclusion, women undergoing treatment with donated sperm are equally fertile regardless of sexual orientation. Therefore, fertility evaluation and decisions on treatment protocol should be made without regard to sexual orientation.

Supplementary data
Supplementary data are available at http://humrep.oxfordjournals.org/.

Acknowledgements
We would like to thank Marie Bladh for her assistance with the tables and figures and her valuable advice as a statistician when designing the SPSS database file. Additionally, we would like to thank selected staff members at all university IVF clinics in Sweden for support in recruiting patients and with assistance in collection of medical and treatment records.

Authors’ roles
S.N., G.S., H.Å., C.L. and A.S.S. participated in the planning and design of the study. S.N., G.S., E.E., C.L. and A.S.S. collected data. Data analysis and interpretation was performed by S.N., G.S., H.Å. E.E., and A.S.S. S.N., G.S., H.Å. and A.S.S. wrote the manuscript. All authors revised the article and gave final approval of the submitted version.

Funding
Funding was granted by the Stiftelsen Familjeplaneringsfonden i, Uppsala; the Swedish Research Council for Health, Working, Life and Welfare; and the Marianne and Marcus Wallenberg Foundation. Funding to pay the Open Access publication charges for this article was provided by Uppsala-Örebro Regional Research Council.

Conflict of interest
The authors report no conflicts of interest, financial or otherwise. The authors alone are responsible for the content and writing of this paper.

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