

Intrauterine donor insemination in single women and lesbian couples: a comparative study of pregnancy rates

I.Ferrara¹, R.Balet² and J.G.Grudzinskas^{1,2,3}

¹Department of Obstetrics & Gynaecology, St Bartholomew's and The Royal London School of Medicine & Dentistry, Royal London Hospital, Whitechapel, London E1 1BB and ²Bridge Centre, 1, St Thomas Street, London SE1 9RY, UK

³To whom correspondence should be addressed at: Department of Obstetrics & Gynaecology, St Bartholomew's and The Royal London School of Medicine & Dentistry, Royal London Hospital, Whitechapel, London E1 1BB, UK

The outcome of intrauterine donor insemination (IUI-DI) with frozen spermatozoa was analysed retrospectively in 675 cycles in single women ($n = 122$; 536 cycles) and lesbian ($n = 35$; 139 cycles) couples. The lesbian patients were younger at the initiation of treatment (mean 34.5 years; range 26–44) than the single women (mean 38.5; range 29–47) ($P = 0.005$). Clinical pregnancy rate was 36% in single women and 57% in lesbians ($P < 0.05$), the cumulative pregnancy rate after six cycles being 47% and 70% respectively, although the outcome was similar when related to age. The miscarriage rate was higher (35%) in single women than in lesbians (15%; $P < 0.05$), the rate being independent of maternal age. There were no apparent differences seen between the two groups with respect to the possible effect of parity, duration of infertility, causes of infertility and type of treatment at initiation of treatment; the sole exception was that the age of lesbian women was statistically significantly younger than that of single women ($P < 0.005$). When corrected for age, the pregnancy rates and complications were lower and higher respectively in single women but these differences did not reach statistical significance. However, the disparity between the treatment outcomes of single women and lesbian patients of similar ages may also reflect the fact that single women are likely to have failed to conceive for a period of time prior to referral to a specialist centre for treatment.

Key words: donor/insemination/lesbian/single women

Introduction

For many years the management of intractable male factor infertility has been successfully achieved by artificial insemination using donor spermatozoa (Deary *et al.*, 1997). Although the definition of 'intractable' has changed drastically due to the development of micromanipulation techniques, there is presently a high public demand for this type of therapy. In recent years requests for assisted reproductive medicine, in particular intrauterine insemination with donor spermatozoa (IUI-DI), have included a sub-group of 'special requests'

mainly from single women or lesbian couples (Englert, 1994; Baetens *et al.*, 1995). Shapiro (1990) reported that, in 1979, 9.5% of physicians performing donor insemination had treated unmarried women. By 1990, this figure had risen to 35%.

The inability to conceive in this group of women is independent of the male factor causes of infertility and they generally cannot be considered to have reduced fertility. A number of studies have considered IUI-DI therapy in both single patients and couples where the partner is oligozoospermic or azoospermic, reporting a pregnancy rate of 13.5% (Kang and Wu, 1996) falling to 6.7% in the presence of other infertility factors (Bordson *et al.*, 1986).

Despite the increasing number of same-sex couples and single women undergoing donor insemination, little information is available on the treatment outcome in these women, the majority of reports addressing ethical considerations (Englert, 1994; Baetens *et al.*, 1995). In addition, some authors have tended to group single heterosexual women and lesbian women under the possibly misleading heading of 'single women' (Bordson *et al.*, 1986; Ahmed Ebbiary *et al.*, 1994).

As we were unable to identify any literature comparing the outcome of IUI-DI in single women and lesbians, we undertook a retrospective analysis of the outcome of the treatment of lesbian couples and single women receiving IUI-DI in relation to age, diagnostic and treatment variables.

Materials and methods

A total of 675 cycles of frozen donor sperm insemination (IUI-DI) was performed on 157 patients, 122 (78%) of whom were single women and 35 (22%) lesbians who attended the Bridge Centre between 1993 and 1997. Typically women who were single or in a lesbian relationship were referred to the Centre for consideration for treatment by IUI-DI. A letter of referral was obtained from the general practitioner in the event of self-referral, seeking information about the general medical and social history. Other information was sought to assess the women's or couples' circumstances in accordance with the Human Fertilization and Embryology Authority (HFEA) regulations concerning the welfare of the unborn child. Women were advised to undergo counselling, an extensive clinical interview and a gynaecological examination. Tubal patency was assessed by hysterosalpingography and/or laparoscopy in women who did not have an unremarkable gynaecological history, had risk factors for tubal disease or those who had failed to conceive within six treatment cycles.

Patients with anovulation were treated with clomiphene citrate (daily for 5 days, 50–100 mg). Ovarian stimulation was used as well empirically i.e. on the woman's request or if pregnancy had not occurred after IUI-DI during spontaneous ovulation to increase the number of oocytes available (Khalifa *et al.*, 1995; Hunges, 1997), with both clomiphene citrate or human menopausal gonadotrophins (Pergonal, Metrodin HP; Serono, Welwyn Garden City, UK; or

Humegon; Organon, London, UK; typically 75–150 units on alternate days) until 2–3 follicles, diameter 16–20 mm, were seen.

In women undergoing ovarian stimulation, transvaginal ultrasonography and serum oestradiol measurements were performed to assess the follicular development and reduce the risk of ovarian hyperstimulation syndrome and the possibility of multiple pregnancy (Haning *et al.*, 1983).

The optimum time for insemination was defined by the determination of the urinary luteinizing hormone (LH) surge by measuring urinary LH (Clearplan-Unipath Ltd, Bedford, UK); ultrasound monitoring was followed by 10 000 IU of human chorionic gonadotrophin (HCG) injection in the stimulated cycles. In stimulated cycles, the insemination was performed ~36 h after HCG injection for single insemination and ~24 h later and 48 h post-HCG in women in whom insemination was performed twice.

Frozen donor sperm samples were thawed, centrifuged and prepared using discontinuous Percoll gradients (Pharmacia AB, Uppsala, Sweden) until January 1996, after which the samples were prepared with IxaPrep (Medicult-Lerso Parkalle 4Z, DK-2100, Copenhagen, Denmark). IUI-DI is the first-intention treatment in our Centre, and this was performed without difficulty in all the women. Clinical pregnancy was confirmed by the detection of a gestational sac by ultrasound, usually at 6–8 weeks gestation.

Statistical analysis

Comparison between successful and failed treatments was performed by application of χ^2 -test followed by Fisher’s exact test when the numerator was <5. The mean values among groups were compared using a standard analysis of variance (ANOVA). Data for life table analysis were analysed by published methods (Cramer *et al.*, 1979). $P < 0.05$ was considered statistically significant.

Results

Pregnancy rates after IUI-DI

A total of 157 patients had 675 treatment cycles, 536 cycles in 122 single women (mean 4.4, range 1–24), the remaining 139 cycles in 35 lesbian women (mean 3.9, range 1–10 cycles). The mean age at the commencement of treatment in lesbian women was 34.5 years (range 26–44), statistically significantly lower than in single women (mean 38.5, range 29–47; $P = 0.005$).

The overall pregnancy rate per patient was 40%, being statistically significantly lower in single women (43/122, 35%) than in lesbians (20/35, 57%; $P = 0.02$), as was the overall pregnancy rate per treatment cycle, being 8% in single women and 14% in lesbians ($P < 0.05$).

Of 63 pregnancies, 55 (87%) occurred within the first six cycles, of which 36 were in single and 19 in lesbian women. After the sixth treatment cycle, only eight women (13%) achieved a pregnancy (seven single women and one lesbian woman). In patients over 40 years old, four pregnancies occurred after six treatment cycles.

Life table analysis of IUI-DI pregnancy rates in single and lesbian women

The cumulative pregnancy rate after eight cycles was 70% in lesbians and 47% in single women, increasing until the eighth cycle in lesbian and the 10th in single women. A statistically significant difference in cumulative probability of pregnancy

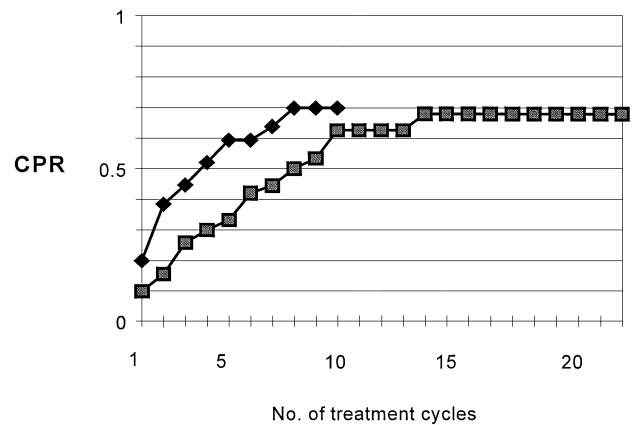


Figure 1. Cumulative pregnancy rate (CPR, %) in lesbian couples (◆) and single women (■) in relation to the number of intrauterine donor insemination cycles.

Table I. Previous obstetric history in relation to pregnancy rates in single and lesbian women

	Single women	Lesbian women
Previous pregnancies	52 (43) ^a	4 (11)
Live births	13 (11)	1 (3)
Termination of pregnancy	31	3
Miscarriage	8	0
IUI-DI previous pregnancies	9 (7)	2 (6)
IUI-DI live births	5 (4)	1 (3)

Values in parentheses are percentages.

^a $P < 0.001$.

IUI-DI = intrauterine donor insemination.

was observed in the two groups ($P < 0.05$) (Figure 1). Pregnancy had not occurred in two women who were still receiving treatment after the ninth cycle. In the majority of cases, women who dropped out of treatment (14 lesbians and 77 single women) did so for personal, social or economic reasons and not because of medical reasons or advice.

Previous obstetric history and pregnancy rate in relation to age

Lesbian women were significantly more likely to be nulligravid than single women; only one of the 35 lesbian patients had had a live birth (resulting from a previous successful IUI-DI treatment), but three lesbian women had reported a previous termination of pregnancy.

Fifty-two (43%) of single women had previously achieved a pregnancy, nine of which followed IUI-DI. Thirteen single women (11%) had had a live birth, (five following IUI-DI). Eight of the remaining 39 women had had a miscarriage, whilst 31 women had a termination of pregnancy (Table I).

Lesbian women were observed to have an apparently higher pregnancy rate (24%) in relation to age at treatment in comparison with single women <35 years of age (12%), but this difference was not statistically significant (Table II).

Table II. Pregnancy rate with respect to age in single and lesbian women

Age (years)	Single women			Lesbian women		
	No. pregnancies	No. cycles	%	No. pregnancies	No. cycles	%
<35	7	61	12 ^a	16	67	24 ^a
35–40	27	256	10	3	50	6
≥40	9	210	4	1	17	5

^a $P = 0.06$ (not significant).

Table III. Pelvic pathology observed at laparoscopy ($n = 35$) and hysterosalpingography (HSG; $n = 132$) in relation to pregnancy rates after intrauterine donor insemination

Pathology observed	Single women ^a		Lesbian women	
	No.	Pregnant	No.	Pregnant
None	13 (37)	3 (9)	5 (14)	1 (3)
Pelvic adhesions	2 (5)	1 (3)	–	–
Endometriosis	8 (23)	2 + 2 (11)	3 (9)	2 (6)
Fibroids	3 (8)	2 (6)	–	–
Endometrial polyp	2 (5)	1 + 1 (6)	–	–
Tubal patency: HSG ± laparoscopy ^b				
Both tubes patent	89 (67)	32 + 1 (22)	22 (17)	15 (11)
One tube patent	17 (13)	6 + 2 (6)	7 (5)	2 (2)

Values in parentheses are percentages of women undergoing the procedures.

^aOne woman had two pathologies.

^bThree single women had only laparoscopy.

Pregnancy rate in relation to pathology observed at laparoscopy and hysterosalpingography

Laparoscopy was performed in 35 patients (eight lesbian and 27 single women), and hysterosalpingography was performed prior to, during and after IUI-DI in 132 patients (29 lesbians and 103 single women). Seven women did not have either procedure, three of whom achieved a pregnancy after the first cycle of IUI-DI, four dropping out before any treatment had begun (Table III). Of the 35 women who had had a laparoscopy, 23 failed to conceive; three patients (two with mild endometriosis and one with endometrial polyp removed before the IUI-DI) conceived twice, two had one miscarriage, one patient with endometriosis had two live births and three women with normal findings had an uneventful pregnancy. The pregnancy rate was 32% (37% lesbians, 44% singles, not significant) and was not significantly different from the overall 35% pregnancy rate of the single women. Pelvic pathology was seen in 14 (52%) of the 27 single women undergoing laparoscopy and in three (37.5%) of the eight lesbian women undergoing laparoscopy. The frequency was not significantly different between the two groups. The only pathology referred to in the lesbian women was endometriosis (38% versus 30%; not significantly different); single women had episodes of pelvic inflammatory disease (PID) and fibroids where lesbian women in our sample had none (Table III).

Pregnancy rate in relation to ovarian stimulation

IUI-DI following spontaneous ovulation was performed in 12 (34%) of lesbian and 49 (40%) of single women, stimulation with clomid was performed in 17 (49%) lesbian and 43 (35%) single women ($P < 0.002$) and gonadotrophins in six (17%) and 30 (25%) respectively (Table IV). Whereas the pregnancy rate was statistically significantly higher in lesbian women following spontaneous ovulation (22% vs 8%; $P < 0.008$) (Table IV), this was not the case after ovarian stimulation.

Miscarriage rate after IUI-DI

Miscarriage occurred in 17 of 63 (27%) pregnancies, occurring less frequently (15%) in lesbian than in single women (35%) ($P \leq 0.05$). One termination of pregnancy was performed in a 35 year old single woman for personal reasons, who subsequently achieved an IUI-DI pregnancy leading to term birth. When adjusted for age, single women appeared to have a higher miscarriage rate in the age group 30–35 years (67% in single women versus 10% in lesbians; $P < 0.05$) (Table V).

Pregnancy outcome after IUI-DI in single and lesbian women

There were no clinical pelvic infections reported during these treatment cycles. Multiple pregnancy occurred in four (6%) single women, all after ovarian stimulation with clomiphene citrate or HMG. The only ectopic pregnancy which occurred was in a single woman. In patients who underwent spontaneous labour, 20% (4/20) did so before 38 weeks (three in lesbian women, all singleton pregnancies and one in a single woman with twin pregnancy). Nineteen women had a Caesarean section. One of the sets of twins delivered at 33 weeks by Caesarean section did not survive. One Down's syndrome baby was delivered in a 39 year old woman who had declined prenatal diagnostic tests to exclude this condition.

Discussion

With the widespread availability of intracytoplasmic sperm injection (ICSI) to couples with male factor infertility, the proportion of single women and lesbian couples seeking and receiving donor insemination has increased, leading to a change in the clientele requesting IUI-DI. In our practice, IUI is used as first intention treatment in DI because of the dramatic improvements in the pregnancy rate achieved in relation to intracervical insemination (Patton *et al.*, 1992). As there is currently little literature relating to the efficacy of this procedure

Table IV. Pregnancy rate following spontaneous ovulation or ovarian stimulation

Therapy	Single women (n = 122)			Lesbian women (n = 35)		
	No. pregnancies	No. cycles	%	No. pregnancies	No. cycles	%
Gonadotrophins	14	134	10	5	24	20
Clomiphene citrate	10	185	5	5	69	7
Spontaneous ovulation	19	217	8 ^a	10	45	22 ^a

^aSignificantly different ($P < 0.01$).

Table V. Miscarriage after intrauterine donor insemination in relation to age in single and lesbian women

Age (years)	Single women (n = 122)			Lesbian women (n = 35)		
	No. miscarriages	No. pregnancies	%	No. miscarriages	No. pregnancies	%
≤30	0	1	0	1	6	17
30–35	4	6	67 ^a	1	10	10 ^a
35–40	9	27	33	1	3	33
>40	1	9	11	0	1	0

^aSignificantly different (Fisher’s exact test: $P = 0.037$).

in these particular patient groups, specifically relating to treatment outcome, we have reviewed our experience in this changing area.

Our analysis has examined the possible effects of age, stimulation regime, previous obstetric history and other factors on treatment outcome in order to determine what may affect the success of IUI-DI in single women in comparison with women in a lesbian relationship.

The higher proportion of single women in our analysis is not intended to reflect accurately the proportions of single women and lesbian couples wishing to conceive in society at large, as lesbian couples may conceive by acquiring spermatozoa from male acquaintances to administer themselves pericervically, thus avoiding medical intervention. In addition, there may be another source of bias in the proportion of single women in relation to lesbians in our study group because some lesbian women may have been classified incorrectly as ‘single women’, perhaps fearing that they may not obtain treatment if their sexual orientation was declared at the fertility unit.

In general, single women in our sample appeared to be statistically significantly older than the lesbian women who were included (mean age 38.5 for single women; 34.5 lesbian. $P < 0.005$). A possible explanation is that the process of deciding to have IUI-DI for single women may take years before acknowledgement that an enduring heterosexual relationship may not occur or that one needs to prepare for the financial and other responsibilities of being a single parent (Cook and Golombok, 1995). Alternatively, most of the women in the lesbian group, having acknowledged their gender preference and being in a relationship, seek to fulfil their wish for a child as a couple and opt to become pregnant without a male partner at a younger age (Polge *et al.*, 1949).

The pregnancy rate observed here was 9.3% (i.e. 63 of 675) for all cycles and 10.2% (i.e. 55 of 539) when only the first six cycles were considered, which is in accord with the rate of 9.7% recently reported in unmarried women treated with IUI-DI (Kang and Wu, 1996). However, when our population was reclassified into lesbian and single women, the pregnancy rate per treatment cycle was statistically significantly higher in lesbian women [14% (20/1390 versus 8% (48/536) in single women; $P < 0.005$], 57% of the lesbian and 35% of the single women achieving pregnancy.

It is reasonable to speculate that lesbian women have a higher fecundability than those women who may have had a heterosexual partner but not conceived. In addition, the heterosexual single women may have delayed seeking IUI-DI, perhaps having tried to conceive prior to referral to a specialist centre. This view is supported by our data in that the single women when compared with lesbian women under the age of 35 appeared less likely to conceive (12% versus 24%; not significant). But this difference was not significant when adjusted for age (Table II).

The incidence of significant pelvic pathology at laparoscopy was similar in both groups, being 52% (14/27) in single and 37.5% (3/8) in lesbian women (not significant). However, laparoscopy was only performed as indicated by gynaecological history or failure to conceive after a number of cycles of IUI-DI. Given the high pregnancy rate in lesbian patients early after the commencement of treatment, the incidence of pelvic pathology can be considered to be less amongst lesbian women. We did not observe any significant differences in pregnancy rates in relation to patency of one or both tubes (Table III) or between single and lesbian women.

Our review of the impact of confounding factors that may,

directly or indirectly, affect pregnancy outcome subsequent to IUI-DI treatment did not show a significant difference in women undergoing ovulation induction and intrauterine insemination in comparison with women treated in unstimulated ovarian cycles, in contrast to observations of many earlier reports (Haning *et al.*, 1983; Patton *et al.*, 1992; Khalifa *et al.*, 1995). However, although an apparently higher pregnancy rate was seen in women receiving ovulation induction with gonadotrophins in comparison with clomiphene citrate, the lesbian women had a higher pregnancy rate than single women when IUI-DI was carried out in a natural cycle (22% and 8% respectively; $P < 0.01$).

The rate of miscarriage in single women was 35%, statistically significantly higher than that seen in lesbian women (15%) and that previously reported (Cramer *et al.*, 1979; Lannou *et al.*, 1995). An increase of miscarriage rate in relation to age has been described in the general population: 15% in women aged 20–29 years versus 46% in women aged 40 years or older (Cramer *et al.*, 1979), a similar high incidence of miscarriage being seen in the overall study population (Table V). However, when considered separately, there was a statistically significant difference seen in the miscarriage rate between lesbian and single women in the age group 30–35 years. The explanation for these findings is not readily obvious but may be related to possible deleterious consequences of heterosexual activity such as low grade chronic infection undetected by routine fertility investigations.

In conclusion, IUI-DI is an effective strategy for single women and women in a lesbian relationship. Pregnancy rates are similar in both groups when corrected for age but lesbian women seem more likely to conceive in the group aged less than 35 years.

Acknowledgements

We gratefully acknowledge the expertise and support of Fiona Foad and her team of embryologists, Alison Bagshawe and medical nursing team at the Bridge Centre.

References

- Ahmed Ebbiary, N., Martin, K., Gibbs, A. *et al.* (1994) Spontaneous ovulatory cycle donor insemination programme: prognostic indicators of a successful pregnancy. *Hum. Reprod.*, **9**, 1852–1858.
- Baetens, P., Ponjaert-Kristoffersen, I., Devroey, P. and Van Steirteghem, A.C. (1995) Artificial insemination by donor: an alternative for single women. *Hum. Reprod.*, **10**, 1537–1542.
- Bordson, B.L., Ricci, E., Dickey, R.P. *et al.* (1986) Comparison of fecundability with fresh and frozen semen in therapeutic donor insemination. *Fertil. Steril.*, **46**, 466–469.
- Cook, R. and Golombok, S. (1995) A survey of semen donation: phase II—the view of the donors. *Hum. Reprod.*, **10**, 951–959.
- Cramer, D.W., Wolker, A.M. and Schiff, I. (1979) Statistical methods in evaluating the outcome of infertility therapy. *Fertil. Steril.*, **32**, 80–86.
- Deary, A.J., Seaton, J.E.V., Prentice, A. *et al.* (1997) Single versus double insemination: a retrospective audit of pregnancy rates with two treatment protocols in donor insemination. *Hum. Reprod.*, **12**, 1494–1496.
- Englert, Y. (1994) Artificial insemination of single women and lesbian women with donor semen. Artificial insemination with donor semen: particular requests. *Hum. Reprod.*, **9**, 1969–1971.
- Haning, R.V. Jr, Austin, C.W. and Carlson, I.H. *et al.* (1983) Plasma estradiol is superior to ultrasound and urinary estriol glucuronide as a predictor of ovarian hyperstimulation during induction of ovulation with menotropins. *Fertil. Steril.*, **40**, 31–36.
- Hunges, E.G. (1997) The effectiveness of ovulation induction and intrauterine insemination in the treatment of persistent infertility: a meta-analysis. *Hum. Reprod.*, **12**, 1865–1872.
- Kang, B.M. and Wu, T.C. (1996) Effect of age on intrauterine insemination with frozen donor sperm. *Obstet. Gynecol.*, **88**, 93–98.
- Khalifa, Y., Redgment, C.J., Tsigotis, M. *et al.* (1995) The value of single versus repeated insemination in intra-uterine donor insemination cycles. *Hum. Reprod.*, **10**, 153–154.
- Lannou, D.L., Gastard, E., Guivarch, A. *et al.* (1995) Strategies in frozen donor semen procreation. *Hum. Reprod.*, **10**, 1765–1774.
- Patton, P.E., Novy, M.J., Burry, K.A. *et al.* (1992) Intrauterine insemination outperforms in intracervical insemination in a randomized, controlled study with frozen, donor semen. *Fertil. Steril.*, **57**, 559–564.
- Polge, G., Smith, A.U. and Parkers, A.J. (1949) Revival of spermatozoa after vitrification and dehydration at low temperatures. *Nature*, **164**, 666–669.
- Shapiro, S., Saphire, D.G. and Stone, W.H. (1990) Changes in American AID practice during the past decade. *Int. J. Fertil.*, **35**, 284–291.

Received on August 19, 1999; accepted on November 16, 1999