Article

Assisted reproductive technologies in public and private clinics

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Abstract

The aim of this study was to analyse the influence of the type of service provided by assisted reproduction clinics. The activities, treatment patterns and results achieved by assisted reproduction centres in Spain were examined, comparing public and private clinics. A retrospective study was carried out using the Assisted Reproductive Technology Register of the Spanish Fertility Society for 2002–2004. The results showed that 74%, 96% and 99% of IVF/intracytoplasmic sperm injection, oocyte donation and preimplantation genetic diagnosis cycles, respectively, were carried out in the private sector. Public clinics performed proportionally more transfers of three embryos than the private clinics (48.1% versus 41.7%). More elective transfers were performed in private clinics. Pregnancy rates per cycle started, per puncture and per transfer were significantly higher among private than public clinics (29.1%, 32.7% and 35.9% versus 25.2%, 28.5% and 32.6%, respectively) ($P < 0.05$). Implantation rate has risen year on year in both types of clinic and was significantly higher ($P < 0.05$), every year, among the private clinics. The multiple-pregnancy rate was significantly higher among the private clinics (30.8% versus 26.4%) ($P < 0.05$). In conclusion, differences exist between public and private clinics as regards to their volume of activity, the range of services offered, clinical practice and results achieved.

Keywords: *assisted reproduction techniques*, *coverage*, *register data*

Introduction

The results obtained by assisted reproduction techniques depend on diverse factors, not only epidemiological (the woman's age, the causes of infertility, etc.) and the clinical practice adopted (pharmacological treatments, the policy regarding embryo transfer, etc.), but also on the social context in which such techniques are applied, although the significance of the role played by each remains unclear (Hearns-Stokes *et al.*, 2000; Pouly and Larue, 2007).

The social context involves a set of social and cultural factors that influence clinical practice and the results achieved by the different healthcare services (Hutayanon *et al.*, 2007; Klemetti *et al.*, 2007; Adisasmita *et al.*, 2008). One of the most important such factors in the field of infertility treatment is the legislation on assisted reproduction, affecting issues such as restrictions on the number of embryos that may be transferred or the treatment given to frozen embryos (La Sala *et al.*, 2008). Other relevant factors in the social context include the existence of competition among clinics (Steiner *et al.*, 2005; Henne and Bundorf, 2008a) and the healthcare coverage available for infertility treatment, which determines the accessibility to such treatment. IVF is costly and, in countries where IVF is offered only in the private sector, its availability depends on a

couple's ability to pay (Neumann, 1997; Stephen and Chandra, 2000). There is evidence that assisted reproduction coverage in the public healthcare sector is related to the results obtained, especially in terms of multiple pregnancies (Jain *et al.*, 2002; Reynolds *et al.*, 2003; Griesinger *et al.*, 2007; Navarro *et al.*, 2008). This finding has been attributed, in part, to the differences observed between assisted reproduction techniques in the USA and in Europe (Gleicher *et al.*, 2006, 2007).

Nevertheless, in previous studies in which the healthcare coverage in different countries has been compared, when a country has been classified as having 'public' coverage, this really includes the results of existing private and public clinics, given the impossibility of distinguishing the titularity of clinics on the basis of existing data records. Thus, although it is true that current national legislation affects all types of clinics, fundamentally with regard to the maximum number of embryos to be transferred per treatment cycle (Jones and Cohen, 2004), there may arise differences concerning the clinical practice applied in each case, which is of great importance for the outcome. For example, while public clinics in many countries have a waiting list and restrictions concerning the age of patients accepted, as well as the number of cycles to be performed per patient (Grupo de Interés de Centros de Reproducción Humana Asistida del Sistema Nacional de Salud, 2002; Tain, 2003; Short, 2007), the private clinics retain total freedom in these aspects. Accordingly, patients may choose to carry out the initial cycles in private clinics while being on the waiting list for the public sector (Malin and Hemminki, 1996; Klemetti *et al.*, 2004).

The aim of this study was to identify this intra-national variability according to the type of coverage available at assisted reproduction clinics. For this purpose, this study compared the activities, treatment patterns and results achieved by assisted reproduction centres in Spain, comparing public and private clinics.

Materials and methods

This is a retrospective exploratory study of the activity registers in Spanish assisted reproduction clinics. The source for the data used in this study was the register of the Spanish Fertility Society for the years 2002, 2003 and 2004 (Marqueta *et al.*, 2006, 2007, 2008).

The register receives data from assisted reproduction clinics, provided on a voluntary and anonymous basis. Among the variables recorded are the forms of ownership of each clinic included. Thus it is possible to analyse the characteristics of the activity and the results obtained at both public and private clinics, within a single national regulatory framework.

The variables analysed were grouped into the following categories: (i) characteristics of the clinic – the level of activity, the range of services offered, and the type of ownership (public/private); (ii) clinical parameters – the average age of the women treated, the cause of infertility and the treatment method adopted; (iii) effectiveness – rates of cancellations and pregnancies; (iv) quality – the numbers of embryos transferred, elective transfers and embryos required to achieve a pregnancy; and (v) safety and risks – multiple pregnancies, hyperstimulation syndrome and embryo reductions.

For the statistical analysis of the results, a bivariate analysis to determine the differences among the study groups was performed using the chi-squared test. In all cases, a level of significance of 5% was applied. The statistical analysis was performed using the Statistical Package for Social Sciences program (SPSS, USA).

Results

The ratio of public/private clinics was similar in the 3 years analysed (**Table 1**). The number of cycles performed per clinic was higher among the public clinics than in the private clinics, with 88% of the public clinics carrying out

Table 1. Numbers of clinics, volume of activity (cycles initiated) and range of services in fresh cycles.

	2002		*2003*		*2004*		*Total*		P-*value*[a]
	Public	*Private*	*Public*	*Private*	*Public*	*Private*	*Public*	*Private*	
Clinics	12 (23.1)	40 (76.9)	13 (17.3)	62 (82.7)	17 (20.2)	67 (79.8)	42 (19.9)	169 (80.1)	–
IVF/ICSI cycles	4083 (25.5)	11,951 (74.5)	5284 (24.4)	16,412 (75.6)	7794 (28.4)	19,687 (71.6)	17,161 (26.3)	48,050 (73.7)	<0.05
Egg donation	62 (2.1)	2830 (97.9)	76 (1.6)	4549 (98.4)	294 (6.1)	4507 (93.9)	432 (3.5)	11,886 (96.5)	<0.05
Cryotransfer	132 (4.5)	2787 (95.5)	303 (7.1)	3979 (92.9)	566 (10.8)	4676 (89.2)	1001 (8.0)	11,442 (92.0)	<0.05
PGD	5 (0.8)	591 (99.2)	12 (1.3)	929 (98.7)	25 (1.8)	1337 (98.2)	42 (1.4)	2857 (98.6)	<0.05
Cryotransfer/ cycle (%)	3.2	23.3	5.7	24.2	7.3	23.8	5.8	23.8	<0.05

Values are number (percentage) unless otherwise stated; ICSI, intracytoplasmic sperm injection; PGD, preimplantation genetic diagnosis.

[a]Chi-squared test for total public versus total private.

Table 2. Treatment procedures for cycle stimulation 2002–2004.

Treatment	*Medication*	*Type of clinic*		P-*value*[a]
		Public	*Private*	
Stimulation	Clomiphene citrate + GnRH	0.0	1.5	<0.05
	HMG	1.3	5.4	
	rFSH	71.8	54.2	
	rFSH + HMG	26.9	38.9	
Constraint	Long agonists	74.8	51.6	<0.05
	Short agonists	4.5	15.5	
	Antagonists	20.5	31.9	
	No analogues	0.3	1.3	

Values are percentages; GnRH, gonadotrophin-releasing hormone; HMG, human menopausal gonaotrophin; rFSH, recombinant FSH.

[a]Chi-squared test for all for total public versus total private.

over 200 cycles per year, versus the corresponding rate of 55% among the private clinics ($P \leq 0.05$). **Table 1** shows that most of the cycles of egg donation and preimplantation genetic diagnosis took place in private clinics. Moreover, the ratio of cryotransfer to IVF-intracytoplasmic sperm injection cycles was significantly higher among the private clinics than among the public clinics (23.8% versus 5.8%).

Table 3. Total and elective embryo transfers in public and private clinics by number of embryos transferred.

Year	*No. of embryos transferred per cycle*	*Total transfers*			*Elective transfers*		
		Public	*Private*	P-*value*	*Public*	*Private*	P-*value*
2002	1	408 (11.5)	1099 (11.3)	<0.05	2/408 (0.5)	232/1099 (21.1)	<0.05
	2	919 (25.8)	3743 (38.6)		171/919 (18.6)	1528/3743 (40.8)	
	⩾3	2234 (62.7)	4851 (50.0)		–	–	
2003	1	530 (12.4)	1648 (12.1)	<0.05	4/530 (0.8)	460/1648 (27.9)	<0.05
	2	1658 (38.8)	6307 (46.2)		185/1658 (11.2)	3769/6307 (59.8)	
	⩾3	2086 (48.8)	5707 (41.8)		–	–	
2004[a]	1	688 (12.6)	2110 (13.5)	NS	53/688 (7.7)	356/2110 (16.9)	<0.05
	2	2695 (49.4)	7805 (50.0)		1591/2695 (59.0)	3860/7805 (49.5)	
	⩾3	2077 (38.0)	5710 (36.5)		–	–	
Total	1	1626 (12.2)	4857 (12.5)	<0.05	59/1626 (3.6)	1048/4857 (21.6)	<0.05
	2	5272 (39.7)	17,855 (45.8)		1947/5272 (36.9)	9157/17,855 (51.3)	
	⩾3	6397 (48.1)	16,268 (41.7)		–	–	

Values are number (percentage).

[a]From 2004, legislation came into force specifying no more than three embryos may be transferred.

Table 4. Pregnancy rates in private and public clinics per cycle, per puncture and per transfer.

	2002		*2003*		*2004*		*Total*		P-*value*[a]
	Public	*Private*	*Public*	*Private*	*Public*	*Private*	*Public*	*Private*	
Cycles	959/4083 (23.5)	3296/11,951 (27.6)	1283/5284 (24.3)	4922/16,412 (29.9)	2090/7794 (26.8)	5776/19,687 (29.3)	4332/17,161 (25.2)	13,994/48,050 (29.1)	<0.05
Punctures	959/3606 (26.6)	3296/10,744 (30.7)	1283/4678 (27.4)	4922/14,711 (33.5)	2090/6932 (30.2)	5776/17,383 (33.2)	4332/15,216 (28.5)	13,994/42,838 (32.7)	<0.05
Transfers	959/3561 (26.9)	3296/9693 (34.0)	1283/4274 (30.0)	4922/13,662 (36.0)	2090/5460 (38.3)	5776/15,625 (37.0)	4332/13,295 (32.6)	13,994/38,980 (35.9)	<0.05

Values are number (percentage).

[a]Chi-squared test, total public versus total private.

On average, patient age was lower in the public clinics than in the private clinics. In the public clinics, 51.4% of the patients were aged under 35 years, 43.7% were aged 35–39 years and 4.9% were aged 40 years or over. In the private clinics, 46.1% of the patients were aged under 34 years, 40.6% were aged 34–39 and 13.3% were aged 40 years or over ($P < 0.05$).

The most frequent cause of infertility among the patients at both the public and the private clinics was male factor. The private clinics tended to make greater use of combination ovulation stimulation (recombinant FSH + human menopausal gonadotrophin) than did the public clinics (38.9% versus 26.9%) ($P < 0.05$) and they made more frequent use of gonadotrophin-releasing hormone antagonists (31.9% versus 20.5%) ($P < 0.05$) (**Table 2**). There were no significant differences between the rates of cycles cancelled between public and private clinics (11.3% versus 10.8%). There were more cases of punctures following which no transfer was performed among the public clinics than among the private clinics (12.6% versus 9%) ($P < 0.05$).

The public clinics carried out proportionally more transfers of three embryos than did the private clinics (48.1% versus 41.7%). Fewer elective transfers, both of a single embryo (3.63% versus 21.6%) and of two embryos (36.9% versus 51.3%) ($P < 0.05$) were performed in public clinics. These differences are due to the clinical practice of embryo transfer applied in the years 2002 and 2003, while a similar one was applied in 2004 (**Table 3**).

The rates of clinical pregnancies per cycle initiated, per puncture and per transfer were higher among the private clinics than among the public clinics (29.1%, 32.7% and 35.9% versus 25.2%, 28.5% and 32.6% respectively) ($P < 0.05$) (**Table 4**). The implantation rate rose year on year at both types of clinic, but was significantly higher ($P < 0.05$), every year, among the private clinics (**Figure 1**). The rate of single-embryo pregnancies was significantly

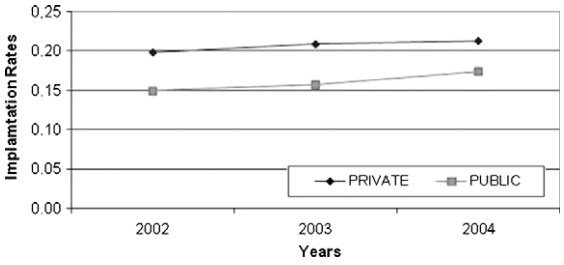

Figure 1. Implantation rates in public and private clinics for years 2002, 2003 and 2004.

Table 5. Singleton and multiple pregnancies in private and public clinics.

Type of pregnancy	*2002*		*2003*		*2004*		*Total*		P-*value*[a]
	Public	*Private*	*Public*	*Private*	*Public*	*Private*	*Public*	*Private*	
Singleton	649/959 (67.7)	2196/3296 (66.6)	947/1248 (75.9)	3272/4811 (68.0)	1281/1699 (75.4)	4050/5646 (71.7)	2877/3906 (73.7)	9518/13,753 (69.2)	<0.05
Twin	243/959 (25.3)	919/3296 (27.9)	263/1248 (21.1)	1339/4811 (27.8)	387/1699 (22.8)	1406/5646 (24.9)	893/3906 (22.9)	3664/13,753 (26.6)	<0.05
Multiple[b]	67/959 (7.0)	181/3296 (5.5)	38/1248 (3.0)	200/4811 (4.2)	31/1699 (1.8)	190/5646 (3.4)	136/3906 (3.5)	571/13,753 (4.2)	<0.05

[a]Chi-squared test, total public versus total private.

[b]Three or more pregnancies.

lower at the private clinics than at the public clinics (69.2% versus 73.7%) ($P < 0.05$) (**Table 5**).

There were no significant differences in the rates of miscarriage between public and private clinics (15.3% versus 16.1%) ($P < 0.05$). Although the percentage of embryo reductions performed at both types of clinics was very low, it was higher among the private clinics than among the public clinics (0.5% versus 0.1%) ($P < 0.05$). The number of cases of ovarian hyperstimulation syndrome recorded was very low and did not vary significantly between the two types of clinic (0.8% versus 0.7%). There was a low incidence of ectopic pregnancies that was not statistically different in public and private clinics (0.1% in both types of clinics).

Discussion

In Spain, as in other countries (Daniels and Taylor, 1993; Nisker, 1996; Neumann, 1997), prioritizing infertility treatments compared with other treatments in health care is a controversial topic. Although public coverage is available for infertility treatment, the private sector predominates in the area of assisted reproduction. In recent years, there has been a slight increase in the share of the public sector, which reflects the effort that is being made in the public sector in facilitating assisted reproduction, in terms of both the volume and the range of the services offered. Nevertheless, these observations reveal this effort to be still insufficient.

Spain leads in Europe in oocyte donations and in preimplantation genetic diagnosis (Nyboe *et al.*, 2008), with these techniques being carried out mainly in the private sector. In order to benefit from these techniques, it is likely that a large number of couples from other countries come to Spain for assisted reproduction health care (Matorras, 2005), mainly due to legal restrictions in these countries (La Sala *et al.*, 2008). Therefore, any study of cross-border fertility treatment should be oriented mainly towards the private sector (Pennings, 2004).

The differences in the average ages of the women treated at the different types of clinics analysed are associated with the inclusion criteria established for the public healthcare sector in Spain regarding this variable (an age limit of 40 years is currently in force) (Grupo de Interés de Centros de Reproducción Humana Asistida del Sistema Nacional de Salud, 2002). Similar limitations have been applied in other countries (Klemetti *et al.*, 2007), a restriction that has been justified on the grounds that IVF resources are scarce and older women have fewer chances of success (Broekmans and Klinkert, 2004) and so it would be wise to concentrate resources on treating younger women with better chances. On the other hand, it can be argued that age should not be a reason to turn women away from IVF, because for older women, IVF may represent their last chance to become pregnant and have a child (Klipstein *et al.*, 2005).

The differences observed regarding the medication utilized to stimulate ovulation may derive from financial reasons, because at the private clinics the patients must pay for the entire cost of the drugs supplied while at public clinics they need only pay 40% of this cost. Private clinics make more use of human menopausal gonadotrophin than recombinant FSH because, for a given level of clinical effectiveness, the acquisition cost is lower (Lloyd *et al.*, 2003). The greater use of antagonists at the private clinics could be related to one or more of the following factors: (i) greater difficulty at public clinics in modifying working patterns, perhaps due to the fact that, as the results show, clinics in the public sector carry out more cycles per centre than do those in the private sector, which makes management more complex; (ii) less vulnerability of public clinics to the influence of pharmaceutical laboratories (Cole, 2006); (iii) due to the limitations imposed on the number of cycles per patient in the public sector in Spain (a limit of two or three cycles per couple), it could occur that patients treated in the public sector in their initial cycles with agonists would carry out subsequent cycles in the private sector with antagonists, as some authors have recommended the use of antagonists as a second choice (Griesinger *et al.*, 2007); and (iv) another factor that should be borne in mind is the greater convenience of antagonists in scheduling cycles, as this could be a crucial issue in small clinics (in the private sector), but not so important in larger ones (mainly in the public sector) with more personnel, in absolute terms.

Although the patients seen at the public clinics were younger than those in the private clinics, the fact that the rate of cancelled cycles did not vary between the two types of clinic could be due to differences in cancellation policies or to the above-mentioned differences in stimulation protocols at the two types of clinic. However, the design of the present study did not enable us to further examine this question.

The transfer policy applied in public and private clinics reflects a reduction in the number of embryos being transferred. The public clinics tend to carry out proportionally more transfers of three embryos and fewer elective transfers, probably because of the limitation on the number of cycles that may be performed at public clinics; this suggests that these clinics seek to maximize the possibilities provided by the fewer opportunities available to their patients. In Spain, from 2004, Law 45/2003 limits the number of embryos to be transferred to three for all clinics. This could explain that the differences in clinical practice of embryo transfer observed in 2002 and 2003 were not observed in 2004. Measures such as those adopted in the Belgian system (fewer embryos, more cycles) would prevent a situation in which the public sector transfers more embryos than does the private sector, thus reducing the rate of multiple pregnancies (Ombelet *et al.*, 2005). On the other hand, the rates of multiple pregnancies in the public sector are lower than in the private sector, although higher than those reported in the European register (Nyboe *et al.*, 2006, 2007, 2008). Patients from the private sector face too strong financial incentives to minimize total treatment costs by conceiving in fewer cycles. As a result, they may transfer more embryos in a given cycle in order to increase their probability of a live birth (Henne and Bundorf, 2008b).

Another factor that has been related with clinical practice in private clinics is that of competition among fertility clinics (Steiner *et al.*, 2005), although Henne and Bundorf (2008a) reported that competition among fertility clinics

does not appear to increase rates of multiple births from assisted reproduction techniques by the promotion of more aggressive techniques.

The number of frozen–thawed cycles increased in inverse proportion to the number of transferred embryos during the period analysed, in both sectors. The lower ratio of frozen–thawed/fresh cycles in the public sector than in the private sector is due to the above-commented higher number of embryos transferred in fresh cycles in the public sector.

The rates of pregnancy achieved in the public clinics were similar to those recorded in the European Register, but lower than those obtained at private clinics in Spain (Nyboe *et al.*, 2006, 2007, 2008). These differences, nevertheless, do not imply that care is less good in one sector than in another. This result could be due to the patients in public clinics having a worse prognosis, as a result of the following factors. First, although the couples treated in the public clinics are younger, they have a longer history of infertility, due to the existence of a long waiting list. This phenomenon is exclusive to the public sector and has been related with poorer results in assisted reproduction techniques (Eijkemans *et al.*, 2008). Second, some women would have their first cycles in the private sector, while remaining on the waiting list in the public sector. This would produce a selection bias, as the couples with a higher probability of achieving pregnancy would be treated in the private sector, and thus the public sector would treat a population with lower possibilities. Third, it is clear that wealthier women selectively opt for care in the private sector. Previous studies have described worse results (Klemetti *et al.*, 2007) and greater risks (Tain, 2003; Dawson *et al.*, 2005) to women from a lower socioeconomic position. Therefore these differences may be related to more serious infertility or a higher prevalence of infertility-related risk factors such as smoking and obesity, which are more common among women from a lower socioeconomic position (Klemetti *et al.*, 2007).

The hypothesis that poor-prognosis patients seek treatment in the public sector is corroborated by a study that analysed the relationship between insurance mandate state and the outcome of assisted reproduction treatments in the USA (Henne and Bundorf, 2008b). These authors suggested that the lower rates of births per cycle and of multiple births per assisted treatment birth observed in US states with a comprehensive insurance mandate are probably due to the fact that reducing the financial burden to patients of assisted reproduction treatment would encourage patients with lower expected benefits to pursue such treatment.

These data indicate that a significantly higher percentage of patients in the public sector who underwent a follicular puncture did not continue with embryo transfer. This can be accounted for by the above-commented poorer prognosis of patients in the public sector or by the fact that oocyte retrieval is performed in the public sector even when ovarian response is inadequate. Therefore, this sector had more cases with fewer oocytes and/or low-quality oocytes that did not finally conclude in embryo transfer. Clinicians in the public sector would seek to maximize the scarce possibilities of these patients, while clinicians in the private sector would rather cancel the cycle and begin another one or resort to a different assisted reproduction techniques (e.g. oocyte donation) in order to reduce costs for the patient.

The observation that there were more embryo reductions in the private clinics is related to the fact, commented above, that the rate of multiple pregnancies is higher in the private sector, and also that this activity is probably not included in the range of services offered in many public clinics.

The results presented should be interpreted taking into account a number of limitations affecting this study. Firstly, as the Spanish register operates on a voluntary basis, those clinics with worse results might abstain from providing their data. We estimate a participation rate of between 25 and 40% of the authorized clinics (Nyboe *et al.*, 2006, 2007, 2008), but the public clinics could be expected to participate more freely in the register regardless of how they performed, as their viability would not be significantly affected by a worsening of results. However, private clinics, which tend to be more concerned about their image, might only participate when results are optimum. Nevertheless, the existence of such a bias is rejected as the levels of participation is similar to the ratio of public versus private clinics recorded in the latest Register of Assisted Reproduction Clinics published by the Spanish Ministry for Health and Consumer Affairs.

Another possible limitation to this study is that, given that the Spanish Fertility Society's register is per clinic and not per cycle, it is impossible to adjust pregnancy rates for confounding variables, such as age, previous treatments, case mix, as is recommended by international experts (Germond and Wirthner, 2008) and done in other registers (Human Fertilisation and Embryology Authority, 2008). Nevertheless, and as commented by Gleicher *et al.* (2007), one can take the position either that there are no valid outcome data available for either the public or the private sector or, as taken for this study, the position that the available data sets are statistically compromised and therefore should be interpreted with appropriate caution.

In conclusion, there do exist differences between public and private clinics as regards the volume of activities, the range of services offered, clinical practice and results achieved. Quantifying the magnitude of these differences and determining the factors involved could help to elucidate the barriers to reproductive care and lead to positive changes – in both the public and the private sectors – in the procedures and resources available for the management of infertility.

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