



## Stress relief after infertility treatment—spontaneous conception, adoption and psychological counselling

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### Abstract

**Objective:** In this study, we sought to evaluate characteristics of couples with spontaneous conceptions after treatment with assisted reproductive technologies (ART). **Study design:** Data from 254 couples who underwent 1127 therapy cycles between November 1987 and February 1997, were analyzed. Chi-Square ( $\chi^2$ ) test and Student's *t*-test were used.  $P < 0.05$  was considered significant. **Results:** Spontaneous pregnancies occurred in 14% of all treated couples. Psychological counselling only was performed in 21% but was observed significantly more frequently among patients without later spontaneous conception. Ten percent of all treated couples applied for adoption. The miscarriage rate was significantly higher in the group of treatment dependent pregnancies compared to the group of patients with later spontaneous conception (27% versus 9%). The spontaneous conception rate differed significantly depending on women's age and normal semen analysis. **Conclusion:** Appearance of spontaneous conception after ART-procedures should be taken into account in the first patient's interview. Depending on women's age and andrological parameters, treatment-success will differ. The positive impact of psychological counselling for stress relief during and after therapy should also be noted, even though a statistically significant impact could not be demonstrated in the present study. Adoption should be discussed as an alternative to overcome infertility.

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### 1. Introduction

It is well established that spontaneous pregnancies after infertility therapy occur even in cases with severe subfertility [1,2]. Most studies focus on treatment-independent pregnancies after in vitro fertilization (IVF) [3,4]. Little is known about the instance of spontaneous conception in couples where different assisted reproductive technology (ART) procedures either succeeded or failed.

Several studies have evaluated interference of psychological adjustment of infertile couples [5,6]. Anxiety, depression, self-esteem, and marital satisfaction were analyzed using different scales and checklists. However, most of these

investigations have focused on the impact of psychological counseling on the success-rate of ART-procedures without regarding the period afterwards. Only a few studies have focused on the employment of psychological counseling after unsuccessful ART treatment [7].

Before intracytoplasmic sperm injection (ICSI) became a standard ART-procedure and gestational surrogacy arrangements were legalized in some countries, adoption and donor insemination were common alternatives for couples with severe male subfertility [8,9]. In some cases, adoption still represents an option for couples after unsuccessful ART treatment [10,11]. Researchers have explored the correlation of stress relief, spontaneous conception, and adoption separately to ART treatment [5,7,12]. However, little information is available concerning the interaction of all three aspects and their correlation to ART treatment. On the other hand women's age, semen analysis parameters, and duration of

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infertility are well known prognostic factors in ART-procedures [13,14] and are therefore also analyzed in the present study.

## 2. Material and methods

Between November 1987 and February 1997, a total of 1127 therapy cycles were performed in 254 couples at an University Medical Center in Germany. These cycles included controlled ovarian hyperstimulation (COH), intrauterine homologues insemination (IUI) with and without ovarian stimulation, IVF with and without ICSI and, in rare cases, gamete intra-fallopian transfer (GIFT). In accordance with the German Embryo Protection Act [15] and the guidelines of the German Medical Association, no donor program in IVF/ICSI procedures was established, a maximum of

intra-fallopian transfer was performed. On average, each couple underwent 4.5 treatment-cycles (range 1–12, S.D. 3.8).

A clinical pregnancy was defined as the occurrence of at least one ultrasonography-confirmed gestational sac (which excludes biochemical pregnancies) with confirmation of positive heartbeats. For IVF and ICSI procedures, the calculation of the clinical pregnancy rate was related to the embryo transfer; for GIFT procedures it was related to gamete transfer. A live birth was described as a treatment cycle that resulted in at least one live born neonate with a minimum gestational age of 25 weeks. Analysis was restricted to only one spontaneous conception per couple. Two study groups were established: those without spontaneous conception after infertility treatment (Group I) and those with spontaneous conception after infertility treatment (Group II). Semen analysis parameters were used as recommended by WHO [16]:

Normozoospermia	Concentration $>20 \times 10^6/\text{ml}$ , motility $>40\%$ , normal morphology $>40\%$
Oligozoospermia	Concentration $<20 \times 10^6/\text{ml}$ , motility $>40\%$ , normal morphology $>40\%$
Asthenozoospermia	Concentration $>20 \times 10^6/\text{ml}$ , motility $<40\%$ , normal morphology $>40\%$
Teratozoospermia	Concentration $>20 \times 10^6/\text{ml}$ , motility $>40\%$ , normal morphology $<40\%$
OAT syndrome	Concentration $<20 \times 10^6/\text{ml}$ , motility $<40\%$ , normal morphology $<40\%$

OAT: oligoasthenoteratozoospermia.

three embryos could be transferred, and fertilized oocytes were frozen in the pronuclear stage.

In this study, cycles with frozen–thawed embryo transfer, azoospermia, and bilateral tubal occlusion were excluded. Two women who changed their partners during the observation period were also excluded.

During the time span nearly 4900 couples were treated at the department. The analyzed treatment cycles were conducted by only one physician from the University Medical Center in order to reduce bias attributable to different treatment-strategies and clinical experiences.

Calculation of women's age was fixed at the beginning of the ART treatment. The follow-up interval lasted 9–60 months and ended in September 1997. After ART-procedures were performed, all couples decided not to continue treatment elsewhere.

The medical records for all 254 couples were analyzed for history of infertility as well as for information following the treatment. In addition, 142 couples completed a detailed questionnaire evaluating resort to psychological counseling and application of adoption. The questionnaire was pre-tested by employees of the department. Eighty-four telephone interviews were conducted using a standardized format, yielding information for a final group of 226 couples undergoing a total of 1005 treatment cycles.

Most of the 1005 treatment cycles were performed as IUI (368) or controlled ovarian hyperstimulation (237). The more invasive treatments were represented by 208 IVF-cycles and 166 ICSI-cycles. In 26 cases a gamete

Chi-Square ( $\chi^2$ ) analysis, Student's *t*-test, and confidence intervals were calculated.  $P < 0.05$  was considered significant. Data entry and analysis were performed using SPSS 9.0 (SPSS Inc.®) software.

## 3. Results

### 3.1. Characteristics of the study population

Women's age ranged from 23 to 43 years with a mean of 33.7 years (Table 1). A statistically significant difference was observed for both groups ( $P = 0.049$ ). Women without a spontaneous conception were older than Group II women (33.9 versus 32.2 years). The highest rate of spontaneous conceptions (44%) occurred in women aged 31–35 years. Men ranged in age from 19 to 62 years, with a mean of 36.1 years. No statistically significant difference was observed between the two groups.

A mean duration of infertility of 3.7 years was observed among all 226 couples and varied from 3.1 (Group II) to 4.0 years (Group I), although this difference was not statistically significant.

Almost three out of four (74%) couples in Group I were found to have primary infertility at the beginning of ART-procedures. The rate was higher for Group II couples (88%) although the difference was not statistically significant. Tubal disease was identified as the main infertility diagnosis for 8% of Group I and for 9% of Group II couples. Severely

Table 1  
Characteristics of the study population

Characteristic	Overall (N = 226)	Group I <sup>a</sup> (N = 194)	Group II <sup>b</sup> (N = 32)	P-value
Women's age (year)	33.7 ± 4.0	33.9 ± 4.0	32.2 ± 3.4	0.049
Men's age (year)	36.1 ± 6.0	36.3 ± 5.4	34.7 ± 5.8	ns
Duration of infertility (year)	3.7 ± 2.7	4.0 ± 2.9	3.1 ± 1.6	ns
Primary infertility	76.1%	74.2% (144)	87.5% (28)	ns
Secondary infertility	23.9%	25.8% (50)	12.5% (4)	ns
Tubal disease	8.4%	8.2% (16)	9.4% (3)	ns
Male factor	29.6%	31.4% (61)	18.8% (6)	ns
Ovulatory disorder	7.5%	7.7% (15)	6.3% (2)	ns
Unexplained	11.9%	11.9% (23)	12.5% (4)	ns
Combinations	31.4%	30.9% (60)	34.4% (11)	ns
Others	11.1%	9.8% (19)	18.8% (6)	ns
Application for adoption	9.7%	8.8% (17/194)	15.6% (5/32)	ns
Application during ART-procedures	45.5%	35.3% (6/17)	80.0% (4/5)	ns
Psychological counseling	20.8%	23.2% (45/194)	6.3% (2/32)	0.029
Counseling during ART-procedures	68.1%	66.7% (30/45)	(2/2)	ns
Normozoospermia	42.0%	39.2% (76)	59.4% (19)	0.032
Oligozoospermia	12.8%	12.9% (25)	12.5% (4)	ns
Asthenozoospermia	9.3%	9.8% (19)	6.3% (2)	ns
Teratozoospermia	2.7%	2.6% (5)	3.2% (1)	ns
OAT <sup>c</sup>	9.3%	10.3% (20)	3.2% (1)	ns
Others	23.9%	25.3% (49)	15.6% (5)	ns

ns: not significant.

<sup>a</sup> Couples without later spontaneous conception.

<sup>b</sup> Couples with later spontaneous conception.

<sup>c</sup> Oligoasthenoteratozoospermia.

reduced sperm quality as the sole infertility factor was described in 31% of Group I couples, compared to 19% of Group II couples. No statistically significant differences were found with regard to infertility diagnoses.

### 3.2. Outcome

Thirty-two out of 226 couples reported a spontaneous conception after ART treatment, indicating a spontaneous pregnancy rate of 14%.

Fifteen treatment-related conceptions occurred in this group (Table 2). Nevertheless, successful ART treatment showed no statistically significant difference in the two groups.

Table 2  
Clinical pregnancy rate in ART procedures

	Overall (N = 1005) <sup>a</sup>	Group I <sup>b</sup> (N = 864)	Group II <sup>c</sup> (N = 141)
Controlled ovarian hyperstimulation	5.5%	5.8% (11/189)	4.2% (2/48)
Intrauterine insemination	7.3%	6.5% (20/310)	12.1% (7/58)
IVF	5.3%	4.8% (9/188)	10.8% (2/20)
ICSI	10.2%	9.1% (14/154)	25.0% (3/12)
GIFT	11.5%	8.7% (2/23)	33.3% (1/3)
Total	7.1%	6.5% (56/864)	10.6% (15/141)

All correlations not significant.

<sup>a</sup> Treatment cycles.

<sup>b</sup> Couples without later spontaneous conception.

<sup>c</sup> Couples with later spontaneous conception.

The outcome of 71 treatment dependent pregnancies showed a miscarriage rate of 27% and a live birth rate of 73% (Table 3). This was a statistically significant difference from the clinical outcome of Group II pregnancies. A lower miscarriage rate (9%) was associated with a higher live birth rate (91%). No ectopic pregnancy or induced abortion was reported.

Group II couples underwent less invasive treatments such as intrauterine insemination or ovarian stimulation more often. IVF was performed in 14% of Group II and 22% of Group I patients. ICSI was performed in only 9% of Group II patients and in 18% of Group I patients. The treatment dependent clinical pregnancy rates demonstrated no statistically significant differences between the two groups (Table 2).

Clomiphene citrate (CC) or human menopausal gonadotropin (HMG) were typically used for controlled ovarian hyperstimulation procedures (426 and 492 of 908 cycles,

Table 3  
Clinical outcome

	ART pregnancies (N = 71)	Spontaneous conceptions (N = 32)	P-value
Live birth	73.2% (52) <sup>a</sup>	90.6% (29)	0.046
Miscarriage	26.8% (19)	9.4% (3)	0.046
Multiple-infant live birth <sup>b</sup>	7.7% (4/52)	0	

<sup>a</sup> The percentages refer to the total number of each column.

<sup>b</sup> All pregnancies were twin pregnancies.

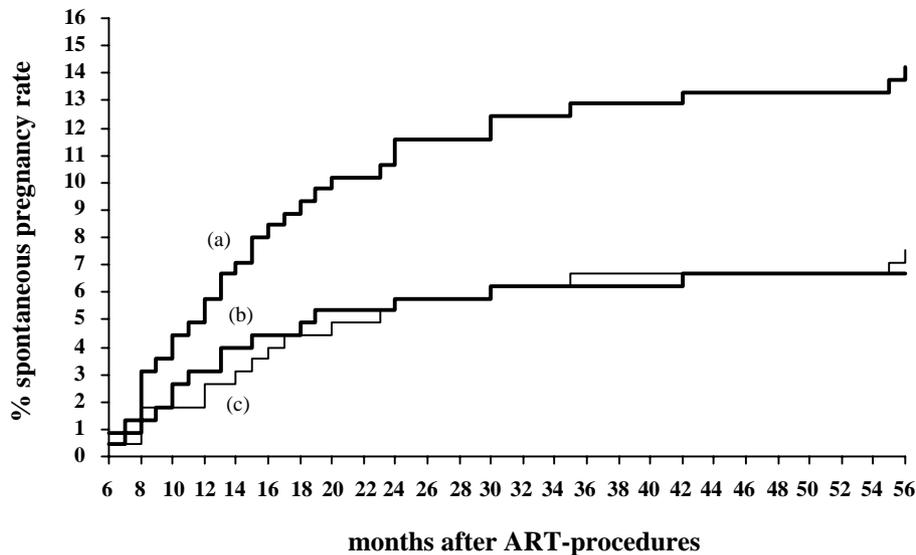


Fig. 1. Cumulative spontaneous pregnancy rate: (a) in all 32 spontaneous conceptions; (b) in couples with former treatment dependent pregnancies ( $N = 15$ ); (c) in couples with no former treatment dependent pregnancy ( $N = 17$ ).

respectively). Gonadotropin releasing hormone-antagonists (GnRh-A) and, in most instances also agonists, were not available during that period. No statistically significant difference was observed in the comparison between the drug therapies for Groups I and II cycles.

The time between the end of ART-procedures and spontaneous conception ranged from 6–56 months, with an average period of 19 months (Fig. 1). Eighty-four percent of the couples with spontaneous conception became pregnant during the first 2 years.

During the first 18 months, 80% of the couples with a former successful ART treatment conceived spontaneously, compared to only 47% of those without a former successful ART treatment. Although the results showed no statistically significant difference, a former successful ART treatment did indicate a positive impact.

### 3.3. Adoption and psychological counseling

Overall, only 22 of all 226 couples (10%) applied for adoption (Table 1), consisting of 17 couples without later spontaneous conception and 5 Group II couples. During ART treatment, four of the five couples with later spontaneous conception applied for adoption, compared to 6 out of 17 couples in the group without spontaneous conception. None of these differences were found to be statistically significant.

Over one in five couples (21%) agreed to psychological counseling (Table 1). This included only two Group II couples (6%) and 45 couples (23%) from Group I, a difference that was statistically significant ( $P = 0.03$ ). Both Group II couples underwent psychological therapy during ART treatment. In Group I, 30 couples (67%) decided to undergo psychological therapy during ART treatment and 15 couples underwent this therapy afterwards. Sixteen percent

of women with treatment dependent pregnancies underwent psychological counseling. This was not statistically different to the Group II couples.

### 3.4. Semen analysis

Comparing results from the first semen analysis performed at the department, normozoospermia was found in 39% of Group I and in 59% of Group II couples, a statistically significant difference ( $P = 0.03$ ) (Table 1). In couples with treatment dependent pregnancies, normozoospermia was found in 47%. This was not statistically different to the group of patients with treatment dependent pregnancies. There were no statistically significant differences observed for other classifications such as oligozoospermia, asthenozoospermia, teratozoospermia, or OAT-syndrome.

Comparing the group of patients with treatment dependent pregnancies and later spontaneous conceptions, no significance was detected with regard to the distribution of normal semen analysis. Among patients with treatment dependent pregnancies, 47% of the tests showed normal results. An OAT-syndrome was found in 10% of Group I and in only 3% of Group II couples.

## 4. Discussion

Improvements in all aspects of assisted reproductive technologies have increased pregnancy rates among sub-fertile couples. For example, in Japan and in France, spontaneous conception after delivery of an IVF-baby was observed in 18 and 9% of couples, respectively [17,18]. Without considering treatment dependent success in an IVF group, a spontaneous conception rate of 7% was reported separately by Roh et al. [19] and Haney et al. [20].

Excluding only bilateral tubal occlusion, spontaneous pregnancies were found among 8% of Israeli couples [3]. Excluding additional azoospermia in an IVF group, a spontaneous pregnancy rate of 11% was determined by Vardon et al. [4]. Without consideration of the preceding ART treatment, Merzoug et al. [2] found 16% treatment independent pregnancies. Hennelly et al. [1] found subsequent spontaneous conception in 21% of couples who underwent successful IVF treatment.

In the present study, spontaneous pregnancies occurred in 14% of all treated couples. This also could be related to patients' work up to avoid unnecessary ART treatments. The quality of diagnostic procedures and characteristics of couples therefore should be evaluated. Women now are older when asking for IVF-treatment. The annual report 1996 of the German IVF Registry demonstrate that IVF-treatment was performed in 29.7% in women aging 35–40 years and in 9.0% in women aging more than 40 years. In 2001, this changed to 32.7 and 10.6%. Health insurances in Germany now are objecting a detailed checklist before paying for an IVF-treatment (for example two sperm-counts in a period of 3 months with fixed limits for morphological criterias are necessary for ICSI-treatment). So the diagnostic pathway now is more standardized.

In the present study, 71 of 226 couples conceived as a result of successful ART treatment. Five factors help to explain the relatively low treatment dependent success rates. First, treatments were performed in a period where new techniques and substances for controlled ovarian hyperstimulation were being introduced and established. Second, a relatively high rate of male infertility (30%) also influenced success rates. Third, ovarian stimulation was employed in only a moderate extent, so that no higher multiple pregnancies occurred. Fourth, legislation in Germany limits the number of transferred embryos to a maximum of three and prohibits embryo selection and donor-programs.

Fifth, a tertiary-care hospital restricted patient selection to a certain group, the majority of whom had been unsuccessfully treated in other reproductive units. Furthermore, there must be a negative bias of patient's selection in the department because the pregnancy rate per transfer in all 7200 IVF/ICSI cycles ranged from 12.0 to 27.2% between 1987 and 1997.

The likelihood of spontaneous conception after ART-therapy is significantly higher in some groups of patients. One of the most important prognostic factors for infertility treatment is woman's age [13]. This was also seen with spontaneous conception in our study, where a statistically significant difference was determined between patients with and without later spontaneous conception. The duration of infertility undoubtedly is related to age but showed no difference between the two groups.

A correlation between successful ART-therapy and the probability of spontaneous conception was determined, as has also been shown by Fadini et al. [21]. Among those with later spontaneous conception, a treatment dependent preg-

nancy rate of 11% was observed versus 7% in the group of patients without later spontaneous conception. Primary and secondary infertility were analyzed at the beginning of ART-procedures. At this time a previous pregnancy seemed not to have any influence on the later spontaneous conception. Secondary infertility with at least one former conception was seen more often in the group without later spontaneous conception and appeared to have no influence, as has also been described by Hennelly et al. [1].

Most of the spontaneous conceptions were observed within a period of 2 years after the termination of ART-procedures [1,3]. This period was similar to 18 months observed within the present study.

An increased rate of miscarriages in women undergoing ART-procedures was described in sundry investigations [22]. In the United States, at least 15% of spontaneous abortions were found in women undergoing ART-procedures [23]. The overall miscarriage rate in the present study was 21%, and showed a statistically significant difference in the two groups. It should be noted that the number of patients was relatively small and the significance was seen as having no great statistical power ( $P = 0.046$ ).

Undergoing an ART-procedure is not usually indicative of signs or symptoms of psychological maladjustment [5]. Nevertheless, for men and women ART-procedures can be stressful [24]. Stress management groups and short courses of psychotherapy during ART-therapy have been described by Brandt and Zech [6] and by McNaughton-Cassill et al. [25]. Poehl et al. [26] described that 18% of a sizeable collective underwent psychotherapeutic counseling and another 10% would commit to undergoing treatment. In the present study, 21% of the couples decided to undergo psychological treatment with a statistically significant difference between the two groups.

Among patients without spontaneous pregnancies, the frequency was significantly higher. A positive correlation between psychological counseling and the occurrence of spontaneous pregnancies after ART-procedures could not therefore be demonstrated in this study. The results could indicate a correlation to longer ongoing infertility and therefore a more stressful non-adjustment to ART therapies. Psychological counseling presented a diversity of therapy techniques so that a detailed evaluation was not feasible.

Seventy percent of the couples started the treatment while undergoing ART-procedures. Although IVF-units in Germany were not committed, at that time, to offering psychological counseling, this altered, so that it became easier for couples to gain this support at the same clinic. Stress relief could be observed not only through acceptance of childlessness, but also by alterations in personal situations [26]. In six couples, spontaneous conception became apparent after they took vacations.

In general, differences in psychological characteristics between couples with and without fertility disorders could not be seen in a study of 564 German couples [27].

Due to the rigorous requirements and extensive delays in the adoption process, most German couples adopt a young child from abroad. German couples probably apply more frequently for adoption due to the restrictions imposed by the German Embryo Protection Act, which does not permit any kind of donor-program to be offered in an IVF-treatment including surrogacy.

In our study, 10% of the couples applied for adoption—nearly half of them in the course of an ART-procedure. Renne entitled his study “There is always adoption” [10]. This seemed to be the motivation for application, even when bureaucratic barriers had to be accepted.

Appearance of spontaneous conception after ART-procedures should be taken into account in the first patient interview. Depending on the age of the woman and the andrological parameters, treatment-successes will differ. Positive impact of psychological counseling for stress relief during and after the procedure also should be noted, even when a statistically significant impact could not be demonstrated in the present study. Adoption as one alternative to overcome infertility should be discussed, assisted by a qualified self-help group or social work agency representative.

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