Attitudes of German infertile couples towards multiple births and elective embryo transfer

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BACKGROUND: In Germany, embryo screening programmes combined with elective embryo transfer are illegal, but there is controversial debate about their legalization. Studies about the attitudes of infertile couples towards multiples, elective embryo transfer and multifetal reduction may help to illuminate how this law shapes patient choices.

METHODS: A survey of 265 German infertile couples was conducted. Different logistic regression analyses were performed to assess independent factors associated with the parity for multiple births, approval for elective embryo transfer and multifetal reduction. RESULTS: Despite prior information about the risk of multiple births, 81% of respondents saw no risk in twin pregnancies and a sizable minority saw no risk even in triplet pregnancies. Eighty-nine percent of the respondents rated a twin pregnancy as desirable, whereas 35% rated a triplet birth as desirable. When presented with a choice of having multiple births versus having no biological children, 99% of the respondents endorsed twins, 84% triplets and 58% quadruplets. Seventy-four percent of the respondents approve of legalizing embryo screening programmes to select a good-quality embryo combined with elective embryo transfer. Ninety-two percent of the respondents rejected fetal reduction of twins. CONCLUSIONS: German infertile couples might conceivably be more willing to accept elective embryo transfer if screening for viable embryos was permitted.

Keywords: multiple births; elective embryo transfer; multifetal reduction; attitudes

Introduction

Trends towards an increasing age of childbearing and an increasing use of assisted reproduction technologies (ART) have contributed to a large rise in the rate of twins and higher order multiple births in recent years. Compared with 1980, the twinning rate in 2001 in the USA was 59% higher, whereas the triplet and higher order (triplet/+) birth rate was 401% higher (Grifo, 2002; Martin et al., 2002). The estimation of Stephen et al. (2002) shows that the number of women experiencing infertility in the USA will range from 5.4 to 7.7 × 10⁶ in 2025 and that many of them will undergo treatment using ART. There is concern that the rates of multiple births will also increase in the course of this trend. The rates of multiple gestations after IVF in Europe and the USA are 26.4 and 35.4%, respectively (Society for Assisted Reproductive Technology; American Society for Reproductive Medicine, 2004; Nyboe-Andersen et al., 2004). In 2005, the German IVF Registry (Jahrbuch des Deutschen IVF Registers, 2005) listed 22.05% twins and 1.30% triplets for IVF treatment.

Multiple births are recognized by the European Society of Human Reproduction and Embryology (ESHRE) Capri Workshop Group (2000), the ESHRE Campus Course Report (2001) and the expert meeting of the Bertarelli Foundation (Bertarelli Spät, 2003) as a major problem associated with both ART and ovulation-induction therapies. For prevention of multiple gestations attributable to ART, the ESHRE Task Force (2007) and the Bertarelli Foundation (Bertarelli Spät, 2003) propose an efficient screening programme of embryos combined with an elective embryo transfer. They recommend replacement of only one good-quality embryo per transfer as the best way of avoiding multiple pregnancies (ESHRE Task Force, 2007).

Today, the transfer of one or two good-quality embryos has become standard in many European countries, and transfer of only one embryo is standard in the Scandinavian countries. Use of this approach is not possible for German infertility physicians, because the German Embryo Protection Law only allows creating three embryos maximum per cycle of IVF or ICSI. Furthermore, usually all the created embryos must be transferred, because creating spare embryos is forbidden under German law. So neither the screening for a good-quality embryo (either morphologically by microscope or genetically by preimplantation genetic diagnosis) nor the cryopreservation of embryos in general are permitted under the German Embryo Protection Law. Moreover, there has been a change in the reimbursement for infertility treatment since 2004 and the
insurance now pays only half of the expenses for three cycles of IVF or ICSI. Despite the restrictive legislation, the change in the reimbursement policy might cause a rise in the rates of multiple births and multifetal reduction in Germany in the coming years. Therefore, German infertility physicians have for a long time pleaded for changing the law. The present trends towards elective single-embryo transfer (eSET) or elective double-embryo transfer (eDET) call for an evaluation of patient attitudes towards multiple births and how patients balance the advantages and disadvantages of elective embryo transfer in IVF/ICSI treatment.

Previous studies have shown: (i) a high preference for twins and a moderate preference for triplets among infertile couples (Gleicher et al., 1995) and (ii) a positive correlation between female age and the desire for multiple births (Gleicher et al., 1995). It must be mentioned though that those surveys date from a slightly earlier era, so the respondents were not informed of the later findings of Thurin et al. (2004) that SET along with a good cryopreservation programme and embryo selection leads to pregnancy rates comparable to those of DET by a significant reduction of multiple pregnancy rates.

Several later studies have shown that the attitudes of the physicians towards eSET have a strong influence on patient attitudes towards eSET. Studies from Finland, where many clinics have implemented eSET policy, reveal that the vast majority of patients will accept eSET if a good cryopreservation programme and embryo selection is available along with reasonable eSET patient selection criteria (younger female age and a maximum of one previous IVF/ICSI cycle) (Hyden-Granskov and Tiitinen, 2004; Tiitinen and Gissler, 2004; Veleva et al., 2006). Pinborg et al. (2003), Murray et al. (2004) and Newton et al. (2007) reveal that infertile couples feared that eSET did not maximize their chances of becoming pregnant. And several studies have shown that a large proportion of infertility patients actually desire multiple pregnancies (Pinborg et al., 2003; Child et al., 2004; Ryan and Voorhis, 2004). It appears that neonatal complications cannot outweigh the desire for an ‘instant family’ (Child et al., 2004). However, no effect of additional information on the acceptability of eSET was found in a study by Murray et al. (2004). Thus it is not given that increasing the level of information would change patient attitudes towards twin pregnancies.

But would German infertile couples accept a clinical policy of efficient embryo screening combined with elective embryo transfer for avoiding multiple pregnancies? Or are there many German infertile couples who desire multiple births—a so-called ‘instant family’—as their preferred treatment outcome? In one of the first large-scale studies conducted on these topics, we assessed the attitudes of German infertile couples towards these issues.

**Materials and Methods**

**Study design and subjects**

The study was approved by the National Medical Ethics Committee and then conducted from October 2003 to January 2005 at the Fertility Center Berlin, a University Hospital Tertiary Level Clinic. All infertile couples being treated at our center were invited to participate in the survey. The respondents were at all stages of treatment: some were primary consultations for infertility, while others were returning for review after one or more treatments. Each man and woman was asked to complete a questionnaire alone and without consulting his or her partner in the same room of the Fertility Center Berlin while waiting for the consultation.

**Pre-survey patient education/counselling**

Prior to participating in the survey, all subjects received the clinic’s standard, obligatory patient education/counselling about ART. This counselling meeting provided practical information about the treatment and background information on the causes of infertility, the indication for IVF/ICSI treatment, hormonal treatment, possible side effects and the chances of pregnancy (including multiple pregnancies, miscarriage, ectopic pregnancies, legal background and numbers of embryo for transfer). Complications related to twin pregnancies were not particularly emphasized; whereas, triplet pregnancies were described in high-risk terminology.

**Survey questionnaire**

We previously conducted 15 intensive qualitative interviews with infertile couples, in order to explore all relevant aspects for the target group. On the basis of those interviews, we constructed a questionnaire and a short information sheet with specific information about the risks of multiple births, i.e. stillbirth, neonatal births and cerebral palsy. The questionnaire and the information sheet were pre-screened for neutrality and comprehensibility in a sample of unselected students of the Free University of Berlin. The questionnaire assessed the respondents’ perception of risk of multiple pregnancies (in respect of twin, triplet and quadruplet pregnancies) on a 5-point scale in which 1 represented ‘very low risk’ and 5 represented ‘very high risk’. For the statistical analysis, we combined the two categories ‘high risk’ and ‘very high risk’ because of the low frequencies of each category in the case of twin pregnancy. For the same reason, we also combined the two categories ‘low risk’ and ‘very low risk’ for the risk perception in the case of a triplet pregnancy.

Treatment outcomes were ranked in order of preference. The possibilities included twin and triplet pregnancies and were ranked on a 4-point scale in which 1 represented a ‘highly desirable’ outcome and 4 represented a ‘quite unacceptable outcome’. For the analysis, we also combined the two categories ‘unacceptable outcome’ and ‘quite unacceptable outcome’.

Respondents were also presented with a choice of having multiple children or having no biological children at all. They were also asked whether they would consider multifetal reduction in a twin, triplet or quadruplet pregnancy. The final question assessed respondents’ opinion about the legalisation of elective embryo transfer. They were offered three possible answers: ‘elective embryo transfer in Germany: (i) should be legalized, (ii) should remain prohibited’ or (iii) do not know’.

**Statistics**

The data were analysed with the Statistical Package for the Social Sciences (SPSS) 14.0. Statistical significance was defined as $P < 0.05$. Frequencies were calculated for responses to questions on attitudes. Separate binary and multivariate logistic regression analyses were performed to examine the predictors of risk perception and the preference and acceptance for multiple births, for embryo screening, and for considering multifetal reduction in a twin, triplet or quadruplet pregnancy. The following six predictive variables were entered into the models: age group ($\leq 29$, $30–39$, $\geq 39$ years), sex, duration of infertility, level of desire for a child, religious affiliation and level of education.
Results

Subjects
The survey was completed by 265 infertile couples, for an acceptable response rate of 87.7%. The females had a median age: 34 years, 25th percentile (30 years), 75th percentile (38 years); the males had a median age: 36 years, 25th percentile (32 years), 75th percentile (40 years). The couples had been undergoing infertility treatment for \( \leq 1 \) year in 9% of the cases, for 1–2 years in 54% of the cases and for \( \geq 2 \) years in 37% of the cases. More information about the sample is summarized in Table 1.

Perception of the risk of multiple pregnancies
When asked to rank the risks of multiple pregnancies, 13% of respondents saw no risk at all in a twin pregnancy, 32% saw only a low risk in a twin pregnancy and 36% saw rather a low risk in a twin pregnancy, 17% saw rather a high risk in a twin pregnancy, 2% recognized a high risk in a twin pregnancy, and no-one considered a very high risk in a twin pregnancy. Compared with this: 2% of respondents saw no risk at all in a triplet pregnancy, 6% saw only a low risk in a triplet pregnancy, 20% saw rather a low risk in a triplet pregnancy, 38% saw rather a high risk in a triplet pregnancy, 27% recognized a high risk in a triplet pregnancy, and 7% considered a very high risk in a triplet pregnancy.

Sex of the partner was independently predictive of the perception of risk of a twin pregnancy [sex: odds ratio (OR) 0.3, 95% confidence interval (CI) 0.1–0.8]. Women underestimated the increased risk of twin pregnancies less often than men. Sex, age, duration of infertility, level of desire for a child, religious affiliation and education were not significant predictors for the perception of risk of a triplet pregnancy.

Legalization of elective embryo transfer in Germany
When asked about the legalization of an efficient screening programme for embryos combined with an elective embryo transfer, 74% of the respondents stated that efficient screening programmes for embryos combined with an elective embryo transfer should be permitted, 11% of the infertile couples supported the prohibition and 15% were undecided. Patients who were Protestant Christians OR 4.35 (95% CI 1.51–12.53) were more likely to disapprove of the legalization of efficient screening programmes for embryos combined with an elective embryo transfer. There was no association with any of the other independent factors.

Discussion
Laws shape people’s behaviours and the choices that they make. In contrast to most other European countries, German law forbids embryo screening, cryopreservation of embryos and creating more than three embryos per cycle of IVF or ICSI. This law was probably written on the basis of a set of lofty moral ideals, without any pragmatic consideration of their real-world impact on people’s choices and health behaviours. By surveying infertile couples about their attitudes,
we attempted to illuminate how their actions respond to the unavailability of these health technologies in Germany.

The basic fact confronting infertile German couples is that they can neither screen individual embryos nor preserve them. They are thus presented with a choice of either transferring multiple embryos or having a higher risk that the single transferred embryo will not lead to a child, thus wasting time and money because only half of the expenses for three cycles of IVF or ICSI are reimbursed by the health insurance companies.

The first survey result to note is that almost all subjects responded that they would rather have twins (99%) or triplets (84%) than have no children at all, and the majority of respondents (58%) even endorsed quadruplets over no children. Moreover, the vast majority (89%) of respondents even considered having twins to be desirable or highly desirable. So in the face of the German Embryo Protection Law, the basic first-thought decision of virtually all infertile couples is going to be transferring multiple embryos, rather than risking a failure from a SET. This is supported by the finding of the logistic regression analysis that the higher the wish for a child is, then the more German infertile couples regard a multiple pregnancy as a desirable outcome.

The second survey result to note is that a large majority (81%) of subjects saw no risk in twin pregnancies and a sizable minority (28%) saw no risk even in triplet pregnancies—despite the fact that all survey respondents had undergone an education counselling session about these risks. As many previous studies showed, patients are overly optimistic about the chances of success with IVF. This optimistic bias may drive a cognitive distortion to see twin pregnancy as a positive, trouble free outcome. Thus in the face of the German Embryo Protection Law, the majority of infertile couples are still likely to run whatever risks there are in order to have the family they want.

The third survey result to note is that if multiple pregnancies did occur, most couples would carry them to term. Virtually none of the couples would elect multiple reduction in the case of twins and a solid majority of respondents would not do so for triplets either. Some German infertile couples may even consider a twin birth as their most preferred outcome because it creates an ‘instant family’, while other German infertile couples with a desire to have more than one child may consider having twins as a way of avoiding more treatments. Thus considered from the angle not of ethics and law but of political policy, the German Embryo Protection Law appears to have the effect of promoting higher rates of multiple births, at a time when European rates of multiple births are dropping.

Our survey also sheds some light on how infertile couples might change their health behaviour if the German Embryo Protection Law was repealed. The survey found that a solid majority (74%) of infertile couples support legalization of embryo screening and elective transfer, while only a small minority (11%) opposes it. Presumably the former group would make use of these health technologies if available and if medically optimal for them; whereas only the latter small group would not consider them. Thus if the German Embryo Protection Law were repealed, the majority of German infertile couples would probably make health choices leading only to single births, rather than having the higher order births often associated with IVF.

The sample investigated here has fairly typical characteristics. Therefore, the results of the study could help redefine the public debate towards the fact that German law still forbids elective embryo transfer, while many other European countries are approaching having it as their standard clinical practice. The restrictive legislation that protects the embryo more than the fetus, in combination with a change in the reimbursement for infertility treatment since 2004, will cause a rise in the rates of multiple births in Germany in the coming years. This can be averted by changing the German Embryo Protection Law, in line with the laws of other European countries.

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