

Attitudes of Infertile Couples to a Multiple Birth: A Review of the Literature and Results from a Survey

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Abstract: Background: Although multiple births are associated with poorer clinical and psychological outcomes, there is a perception that couples choose multiple embryo transfer because they would prefer a multiple IVF birth.

Objective: To review literature concerning the attitudes of infertile couples to a multiple birth and to explore factors influencing couples' decisions about embryo transfer.

Methods: Thirteen research articles were identified in the medical literature that examined women's choices concerning multiple IVF pregnancies. A cross-sectional survey was conducted at one centre for the treatment of infertility in the East Midlands, UK. Sixty-eight couples undergoing *in-vitro* fertilisation (IVF) with at least two embryos available for transfer were recruited to the study. Outcome measures were couples' ratings of factors influencing the number of embryos transferred.

Results: Eight of the 13 studies found couples favouring a multiple birth to be in the majority. Most studies, however, had required hypothetical or retrospective judgments. In the present survey no patient had chosen single embryo transfer (SET), 56 (76%) had had 2 embryos transferred and 16 (24%) had 3 embryos transferred. Patients strongly perceived that SET would reduce the chances of having a child. Only 13 women (19.1%) considered that a desire for twins had influenced their decision. Of more importance was the desire to increase the chance of pregnancy (92.7%), the medical advice received (91%) and a desire to avoid further treatment (57.3%). The majority of couples found the decision regarding embryo transfer easy but a third would have liked more information. Participants with children were less likely to report a desire for twins ($p < 0.06$) but other demographic factors had no influence.

Conclusions: Although the literature has suggested that infertile couples have strongly positive attitudes to multiple pregnancies, most patients are not seeking a twin birth when they choose multiple embryo transfer and physicians have an important role to play in helping patients make informed decisions.

Keywords: Single embryo transfer, IVF, patient decision making, double embryo transfer.

BACKGROUND

Although there have been recent moves across Europe to limit embryo transfer to a maximum of two embryos (DET) per cycle of *in vitro* fertilisation (IVF), rates of twins remain high at around 25% of births [1]. Multiple births are associated with increased medical risks for both the mother and infant [2]. There are also increasing concerns about their impact on maternal mental health [3-6] and the considerable economic demands they can place on overstretched health services [7, 8]. A further, frequently overlooked, consideration is the significant social and economic disadvantage that couples can experience following a multiple birth [5, 9]. For example, in one prospective study only 44% of women with a multiple IVF birth had returned to work in the year following delivery, compared to 73% of women with a single IVF birth [5]. Such economic considerations are likely to be increasingly important as IVF treatment continues to become more available.

The medical, social and psychological risks associated with higher order births and convincing evidence to support the effectiveness of elective single embryo transfer (eSET) in selected women [10-12], has led to the routine implementation of eSET both in Belgium and Scandinavia [13]. More recent work has suggested that even in women aged 36-39 years, where frozen embryos are used, eSET has a significantly higher cumulative pregnancy rate than double embryo transfer (DET) [14]. The practice has not found support in the US or other countries in Europe, including the UK, possibly due to the belief that prospective parents have a preference for DET and a multiple birth, and a conviction that this preference should be paramount [15]. A review of the literature on attitudes towards a multiple birth, however, shows the issue to be more complex than a simple desire for a multiple birth, with many other factors playing a part (See Table 1 for a summary of findings).

Research looking at attitudes towards multiple births began in the 1990's when Leiblum and colleagues confirmed their hypothesis that after years of failure to conceive infertile women would be more receptive to the idea of a multiple birth than fertile women [16]. This was followed by

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Table 1. Preference for a Multiple Pregnancy in Infertile Women

Authors	Year	Sample Size	Country	Question/Scenario	Timing of Question	Preference for Multiple Pregnancy
Leiblum <i>et al.</i>	1990	51	USA	Percentage of women responding "would like to have more than one child in a single pregnancy?"	During participation in University hospital IVF program	89.8%
Gleicher <i>et al.</i>	1995	582	USA	Percentage of couples responding "we would have loved to conceive twins"	During treatment or <1 year after treatment at Centre for Human Reproduction	67%
Goldfarb <i>et al.</i>	1996	27	USA	Women's favourability rating for twin outcome	On entering University hospital IVF treatment program	4.5 ⁺
Murdoch	1997	150	UK	Percentage of couples responding "one baby" the ideal outcome of IVF treatment	Survey of CHILd support group, 30% of respondents had conceived.	31%
Grobman <i>et al.</i>	2001	200	USA	Percentage of women rating twins desirable or very desirable	Attending hospital infertility clinic, at different stages of treatment.	66.5%
Pinborg <i>et al.</i>	2003	870	Denmark	Percentage of mothers wishing for twins as the first child	IVF/ICSI mothers of twins and singletons who gave birth in 1997	62.3% (singletons) 84.7% (twins)
Kalra <i>et al.</i>	2003	90	USA	Percentage of women rating twin pregnancy most desirable outcome	Attending university based infertility clinic	38%
Ryan <i>et al.</i>	2004	449	USA	Percentage of women rating twin or multiple pregnancy as preferred outcome	New patients at 3 clinical sites presenting with infertility	20.3%
Child <i>et al.</i>	2004	460	Canada	Percentage of women saying twins ideal number with next fertility treatment	Attending university hospital fertility clinic	38.9%
Murray <i>et al.</i>	2004	200	UK	Percentage of couples responding no to "would you prefer a single baby?"	Attending Assisted Reproduction Unit for first IVF cycle	38.5%
Steures <i>et al.</i>	2005	40	The Netherlands	Percentage of couples wishing to continue even if 100% chance of multiple pregnancy	First visit to gynaecologist for sub-fertility	77%
Blennborn <i>et al.</i>	2005	137	Sweden	Percentage of women having 2 embryos transferred	After embryo transfer	58.8%
Porter & Bhattacharya	2005	12	UK	Number accepting the possibility of twins as outcome of DET	On waiting list for IVF treatment	12 (100%)

⁺ Mean rating (1 very unfavourable - 5 very favourable)

the widely reported study by Gleicher and colleagues: one of the first investigations of the attitudes of infertility patients themselves [17]. This survey of 3800 couples receiving treatment for infertility found of the 582 couples who responded 67% expressed a desire for the conception of twins. The desire for twins was significantly positively correlated with the couples' age. In addition the authors argue that although couples indicated an awareness of the increased risk of a twin birth they did not view it as a major concern. Another study in the 1990's attempted to explore differences in couples' attitudes by asking each partner to complete a self-report questionnaire independently [18].

They found all the women expressed favourable or very favourable attitudes towards twins and that they rated twins significantly more favourably than did their male partners.

The majority of this early research was carried out in the USA however, one study appeared to find favourable attitudes in the UK too during a survey of all members of CHILd (a support group providing support and information to people undergoing infertility investigations or treatment in Great Britain) in 1997 [19]. The authors received 150 replies to the question "what is the ideal outcome of IVF treatment", of these only 31% of couples answered "one child". The majority of couples (64%) were also prepared to consider

selective reduction of higher order multiple pregnancies so that more embryos could be replaced to increase the chance of pregnancy. However, 30% of these respondents had conceived after IVF and of these 30% had had a twin birth; their replies may just be justifying decisions already taken. Support for this can be seen in the findings of a Danish study which looked at the attitudes of IVF mothers of twins towards twins and single embryo transfer, and compared them to a control group of IVF singleton mothers and mothers of naturally conceived twins [20]. Two thirds of the IVF mothers disagreed with single embryo transfer and significantly more preferred twins as their first delivery compared to the IVF singleton mothers or the mothers of naturally conceived twins. With only 3.8% saying they considered the additional risks of a twin pregnancy to be a problem, IVF mothers of twins showed a reluctance to see a twin pregnancy as a complication. The authors suggest risks may be minimized or even denied, in support of which the only significant predictor of acceptance of single embryo transfer was delivery of a child with very low birth weight; these mothers had been forced to experience the possible complications of a multiple pregnancy.

A prospective study by Grobman and colleagues found that although 67% of the 200 women attending an American infertility clinic expressed a desire to conceive a twin pregnancy they were not able to accurately estimate the risks of such a pregnancy [21]. Moreover, when women were given the actual probabilities of certain perinatal complications associated with a twin pregnancy, such as delivery of an infant weighing less than 1500 g; their attitudes became significantly less favourable. This is in contrast with the study by Gleicher and colleagues which claimed women were educated about the risks of a multiple pregnancy [17]. However, this was only assessed by responding to the question "A twin delivery carries a significantly increased (or very little additional) risk to mother and babies", which allows for an individual interpretation of the risks involved, moreover answers were not clearly affirmative or dismissive of these statements [21]. Interestingly Grobman and colleagues found that although 89% of the women who had IVF reported being counselled regarding the risks of a multiple gestation, it did not significantly affect their estimate of the complications associated with a multiple gestation. In an extension to this study researchers reported on differences and similarities found in the responses of 90 couples who took part and were interviewed individually. Although the majority of women (68%) and their partners (64%) rated a twin pregnancy as desirable there was some disagreement between the couples as for 21% only one partner believed a twin gestation to be the most favourable outcome [22]. Despite increased media coverage and interest in the debate about multiple births more recent studies also report couples preferring a multiple birth with 41% of patients (at all stages of treatment) attending a fertility clinic in Canada during 2000 desiring a multiple birth as the outcome of their fertility treatment [23]. Factors increasing the desire for a multiple birth were increasing length of infertility or previous cycles of assisted reproductive treatment which the authors suggests indicates the desire for an 'instant family'. Patients with children already and those recognizing the increased foetal risks of a multiple

pregnancy were significantly less likely to want a multiple birth. The authors argue that as the only significant variable associated with recognition of increased foetal risks of a multiple birth was previous assisted reproductive treatment and that during clinic appointments and counselling sessions patients are informed of the risks of a multiple pregnancy this indicates the potential role patient education could play in reducing the desire for a multiple birth.

Another recent study found that 20% of new infertility patients surveyed at three clinics in Iowa during 2001 to 2002 ranked a multiple pregnancy as their preferred treatment outcome compared to a singleton pregnancy [24]. Although most women knew of the increased risk of preterm delivery and increased pregnancy and delivery risks for the mother with a multiple pregnancy, they were less well informed about the risks of cerebral palsy and infant mortality with less than half indicating they knew of these. The desire for a multiple birth was found to be associated with a number of patient characteristics: null parity, lower family income, younger patient age, previous evaluation for infertility, limited knowledge of the outcomes of a twin gestation and a longer duration of infertility. The authors argue clinicians should be able to influence patient knowledge, particularly as these patients were generally of a high socioeconomic and educational status.

Couples attitudes towards multiple births have also been explored in relation to their attitudes towards eSET. A recent UK study asked couples about the acceptability of a hypothetical policy of eSET, their knowledge of the risks associated with a twin IVF pregnancy, how many embryos they would like transferred and how they felt about a twin pregnancy; as part of a study looking at ways of better informing couples about the risks of a multiple birth [25]. They found only 38.5% of couples responded "no" to the question "would you prefer a single baby?", however, over 90% of each group also said they would not mind having twins, and over 70% of all the couples said they would like 2 embryos transferred. Providing couples with extra information did not influence acceptance of a hypothetical policy of eSET with couples only prepared to accept it if pregnancy rates were unchanged. The study suggests couples' main aim is to achieve a pregnancy and rather than desiring a twin birth they are prepared to accept one in order to achieve a pregnancy.

A study by researchers in the Netherlands looked at acceptance of the risk of a multiple pregnancy in couples attending for their first visit to a gynaecologist for sub-fertility [26]. They found that even when presented with a 100% risk of a multiple pregnancy 77% of couples chose intrauterine insemination in preference to expectant management. A Swedish survey of couples following embryo transfer found that, despite good information about the risks of a multiple pregnancy and the physician's positive attitude towards eSET, only a third of the couples with at least 2 available embryos opted for eSET [27] but for those who did nearly 70% reported that their decision had been influenced by the possibility of having twins. Interestingly, the most commonly reported factor to have strongly influenced the couples' decisions in both the eSET and DET groups was physician's advice. A very recent qualitative study exploring

patients attitudes towards eSET found all the 20 couples taking part in the semi-structured interviews had discussed the possibility of twins and although not expressing a preference for twins were happy to accept the possibility, believing DET increased the chance of pregnancy [28].

In summary, research does appear to suggest that multiple births are rated as highly desirable by many infertile women [16-18, 20, 21, 26-28], though preferences may not be accurately assessed where studies require hypothetical or retrospective judgments. Furthermore, couples often have poor levels of knowledge concerning the risks associated with a multiple birth [24] and are therefore unprepared to make informed choices about eSET. This may reflect the ambivalence of health professionals to the issue. A recent opinion piece has argued strongly against viewing a twin birth as a complication, on the grounds that most twin births are healthy and that couples positively prefer a twin birth [15]. This rather narrow perspective clearly ignores the well documented social and psychological impact of a multiple birth [5] and the limitations of the literature examining couples' preferences.

Information alone may not be sufficient, however, to increase uptake of eSET. A recent Swedish survey of couples following embryo transfer found that, despite good information about the risks of a multiple pregnancy and the physician's positive attitude towards eSET, only a third of the couples with at least 2 available embryos opted for eSET [27]. There is a need, therefore, to examine more closely the factors which drive couples' preferences for DET [24]. Arguably studies should not require hypothetical or historical judgments and could be conducted in a variety of treatment settings, including those that do not actively promote eSET. This study aims to contribute to the debate concerning couples' decisions regarding embryo transfer.

METHOD

Design, Participants and Procedure

Women undergoing embryo transfer and their partners attending one UK centre for assisted reproduction between 9th October 2003 and 6th January 2004 were recruited to this cross-sectional survey if they were English speaking. The anonymous questionnaire obtained basic demographic details and information concerning the present cycle of IVF including relevant fertility history. Respondents were asked to rate a list of factors according to whether each factor had been a major factor, a strong factor, a minor factor or not a factor in the decision regarding the number of embryos to transfer. They were also asked to indicate their agreement to a statement that probed their perception of the impact of eSET on treatment outcome. Male and female partners completed the questionnaire independently and returned them in separate sealed envelopes before leaving the unit.

Ethics

The study conformed to Human Fertilisation and Embryology Authority guidelines and approval for the study was granted by CARE Fertility Centre Ethics Committee.

RESULTS

Response Rates

During the study period questionnaires were distributed to 110 women. Seventy-two women out of 110 (65%) returned the questionnaires of whom 3/72 were excluded because only 1 embryo was available for transfer and 1/72 was excluded because information regarding embryo transfer was missing giving a final sample of 68. Information from male partners was available for 60/68 women. Demographic and clinical characteristics of the sample are shown in Table 2.

Table 2. Demographic and Clinical Characteristics for Female Partners

Demographic or Clinical Variable		Number of Responses
Mean age (SD)	36.0 (4.35)	68
Mean age of partner (SD)	38.4 (6.02)	68
Educated to degree level	30 (45.5%)	66 ^a
Mean years trying to conceive (SD)	5.2 (4.16)	68
Female partner has children	14 (21%)	68
Male partner has children	20 (31%)	68
First embryo transfer	33 (48.5%)	68
Median number of eggs available for transfer (range)	3.5 (2-11)	68

^adata missing for 2 participants

No couple had received single embryo transfer. Seventy-six percent of women had had 2 embryos transferred (52/68) with the remaining 16 women having 3 embryos transferred. However, only 13 women (19.1%) considered that this decision was influenced by a desire for twins. Of much more importance was the desire to increase the chance of pregnancy (92.7%), to avoid further treatment (57.3%) and to avoid the cost of further treatment (38.2%) (Table 3).

Although there was statistical agreement between couples in whether they wished for twins the Kappa value was 0.5 indicating only moderate concordance. Women who rated desire for twins as a strong factor in their decision regarding embryo transfer did not differ from other women in the sample in terms of age, educational level, years of infertility, or number of previous IVF cycles but they did have fewer children ($Z=2.2$, $P=0.056$) with none of the women with previous children reporting a desire for twins as an important factor (Fisher exact probability <0.06). There were no significant differences for men. The majority of women (48/64) and men (39/59) strongly agreed that the decision regarding embryo transfer had been easy to make but in 23 couples (34%) at least one of the partners would have liked more information regarding the decision about embryo transfer. Nine couples expressed a desire for more statistics, particularly success rates relating to number

Table 3. Factors Having a Strong or a Major Influence on the Decision Regarding Number of Embryos Transferred

	Women (n=68)	Men (n=60)
Medical advice	62 (91.2%)	51 (85%)
Wish to increase chance of pregnancy	63 (92.7)	57 (95%)
Desire to avoid further IVF treatment	39 (57.3%)	30 (50%)
Desire to avoid cost of further treatment	26 (38.2%)	22 (36.7%)
Ethical or religious considerations	2 (3%)	1 (1.7%)
Desire for a twin birth	13 (19.1%)	12 (20%)
Desire for a triplet birth	3 (4.4%)	4 (6.7%)

of embryos transferred and two couples would have liked more time to discuss the decision.

Single embryo transfer was considered to reduce the probability of successful outcome of treatment with 39/68 women and 39/60 men strongly agreeing that replacing one embryo when two embryos were available would reduce the chance of having a child.

DISCUSSION

Previous research has suggested that infertile couples have a positive preference for a multiple birth, but evidence from this study suggests that the primary motivation for double or triple embryo transfer is to maximize the chance of pregnancy rather than increase the probability of twins or triplets. This was particularly true for women with existing children, none of whom wished for a twin birth. There appears to have been strong feelings in the group as a whole that the clinically preferred option was to replace two or more embryos and an overwhelming perception that replacing two embryos would definitely increase their chance of becoming a parent. Around half of couples in the study were undergoing their first cycle of IVF and may well have underestimated the probability of conceiving twins. A recent randomized controlled trial comparing eSET and DET in women who were less than 35 years of age and receiving their first IVF cycle, found that of the 19 (36%) women in the DET group with a live birth, 7 (37%) had twins [11].

Three quarters of participants had found the decision regarding embryo transfer easy to make which suggests that the majority may not have fully appreciated the complexity of the decision that they were making. Recent qualitative research found that couples in a Scottish fertility centre had received little information about the risks associated with twins and tended to be unconcerned about the implications either for themselves or for infant health [28]. This was echoed in the present study, with over a third of couples reporting that they needed more information, particularly statistical information about outcomes. Better knowledge of medical risks associated with a multiple birth has been found

to be associated with a reduced desire for twins [24] and patient education has a role to play in reducing rates of multiple births [13]. However, a randomized controlled trial of additional information regarding complications associated with a twin birth failed to increase the acceptability of eSET [25], regardless of whether the information was provided by leaflet or by a counselor. Blennborn also found that a surprisingly small proportion (37%) of female partners opting for eSET had been influenced by the medical risks associated with a twin birth [27].

The present study confirms the conclusions of previous research regarding the strong influence of physician advice for patient decisions about embryo transfer [19 27]. A multiple birth represents a serious side effect of IVF and undoubtedly "physicians should provide couples with comprehensive information to enable them to make more realistic decisions" (p 137) [29]. With ever higher rates of infertility forecast, it is timely that research should also address the attitudes and knowledge of the physicians and embryologists providing that information. There is some evidence in the literature [28], which was supported by our own observations, that health professionals involved in infertility treatment believe that couples positively seek a multiple birth and that a twin birth therefore represents a bonus. Clinicians' awareness of the consequences of a multiple birth and their ability to convey statistics in a form which can be easily understood are likely to be key factors in patient acceptance of single embryo transfer [30 31]. Successful approaches might also highlight the advantages of a single birth rather than simply focusing on the risks of a multiple birth. For example, recent evidence suggests that singletons born after eSET are heavier than singletons born after DET [32] and our own qualitative research found that twice as many mothers of singletons were likely to express extremely positive emotions in the early weeks after birth compared to mothers of multiples [33]. If, as suggested by a recent German study [34], the majority of couples view two-children as the ideal family size, then more emphasis on the value and effectiveness of sequential eSET could serve to reduce the number of multiple IVF births without compromising patient choice.

STRENGTHS AND WEAKNESSES OF THE STUDY

The survey did not probe couples' perceptions of risk associated with a multiple birth as it was felt to be unethical to do so at such a sensitive stage of treatment. A possible limitation is that only couples from one private fertility centre were sampled, but the centre does draw from a wide referral base suggesting that that our sample is likely to reflect the broader population seeking fertility treatment in the UK. The study was strengthened by the use of an anonymous questionnaire at the point of embryo transfer thus ensuring honest and accurate answers whilst minimizing recall bias.

CONCLUSION

The results of the study suggest that most couples choosing DET are not motivated by a desire for twins and highlighted the important role that clinicians have to play in enabling patients to make informed choices about multiple embryo transfer.

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