



Review

Multiple births following in vitro fertilization treatment: redefining success



A. Umranikar^{a,*}, D. Parmar^b, S. Davies^a, S. Fountain^a

^aSalisbury NHS Foundation Trust, Salisbury, UK

^bPeninsula College of Medicine and Dentistry, Plymouth, UK

ARTICLE INFO

Article history:

Received 5 November 2012

Received in revised form 13 March 2013

Accepted 24 June 2013

Keywords:

In vitro fertilization

Assisted reproductive technologies

Multiple births

Embryo transfer

ABSTRACT

The focus of this article is to review the definition of success following in vitro fertilization (IVF) treatment. Pregnancy rates after IVF have been increasing, but the problem of multiple births with its associated morbidity and mortality has been considerable. This has led to rethinking of assisted reproductive technology (ART) success not only in terms of live birth rates, but also in terms of reduction of multiple births to singleton babies. Single embryo transfer using blastocysts and such other measures are being encouraged. Financial factors and patient satisfaction are key issues. IVF success is thus being redefined.

© 2013 Elsevier Ireland Ltd. All rights reserved.

Contents

1. Introduction	299
2. Prevalence of multiple births: scope of the problem	300
2.1. Problems associated with multiple births	300
3. Strategies to reduce multiple births	300
3.1. Acceptance of eSET so far	300
3.2. Blastocyst transfer	301
4. Challenges faced in the transition period prior to implementing the SET policy	302
4.1. Financial challenges	302
4.2. Patients' expectations and attitudes	302
5. Conclusion	303
References	303

1. Introduction

Infertility affects 1 in approximately 6 couples. Growing awareness and increased availability of fertility services have resulted in many couples opting for in vitro fertilization (IVF) treatment. Since the first successful IVF in humans in 1978, IVF has become a standard treatment for subfertility [1]. There have been remarkable achievements over the years in pregnancy success rates following IVF. This has been due to continuous improvement in ovarian stimulation protocols, and refinements and advances in

IVF laboratories resulting in improved embryo quality. In addition to the success rates achieved through IVF and intracytoplasmic sperm injection (ICSI) treatment, there has been an intense effort to reduce the incidence of multiple births in recent years.

IVF success has been defined as a live birth after an assisted reproductive technology (ART) cycle, regardless of the number of live-born infants per delivery [2]. This definition needs to change as we take into consideration problems related to multiple births including costs and other constraints. In the reporting of ART success rates, commercially competitive settings may maximize numerators and minimize denominators [3]. One may measure success rates in terms of clinical pregnancy (evidence of sac, detection of fetal heartbeat) or more ideally live birth rates, but the problem is complex. Multiple pregnancies can be associated with detrimental outcome. It is time that success is defined in terms of

* Corresponding author. Tel.: +44 2380262392.

E-mail addresses: aarti.umranikar@salisbury.nhs.uk, drsaumranikar@hotmail.com (A. Umranikar).

not only live birth rates but also the rate of multiple births. This review attempts to address some of these relevant issues, with special reference to the UK and Europe.

2. Prevalence of multiple births: scope of the problem

There have been growing concerns over the incidence of multiple births following IVF. IVF is often a costly decision for patients financially, medically and emotionally and this is especially so when it is associated with multiple births [4]. The overall incidence of multiple births has been on the rise over the past 30 years. This is mainly attributable not just to the increasing use of IVF treatment by subfertile couples, but also to the increasing age of women seeking fertility treatment and to delayed childbearing [5,6]. The majority of the multiple births are twins, as the rate of triplet pregnancies has reduced over the last decade. While the incidence of multiple births is just over 1% (1.25%) following natural conception, the figure rises to 24% with IVF treatment. In the UK around 11,000 babies are born every year through ART, contributing to around 2% of live births [7].

In the UK the Human Fertilization and Embryology Authority (HFEA) [7] collects records of approximately 50,000 fertility treatments performed every year. Around 1 in 4 twins born in the UK are as a result of IVF treatment [7,8]. Around 50% of these are born before 37 weeks and contribute to nearly 10–20% of all low birth weight babies [9]. Until 2008, the rate of multiple births related to IVF was 26.7%. This reduced to 22% in 2009 following an increase in uptake of elective single embryo transfer (eSET) policy. The highest proportion (31.2%) of multiple births was seen in women between 18 and 34 years.

There has been a similar increase in twin pregnancies following IVF treatment in most countries in Europe, Scandinavia, United States, Canada and Asia. In Denmark, the twin birth rate increased from 17.8 to 22 per 1000 births between 1996 and 2003. In Sweden, twin births increased 1.9-fold from 1973 to 2000 and in Norway the increase was 2.2-fold from 1974 to 2002 [10]. Studies from Australia have shown a greater than 20% risk of twins or higher order multiple pregnancy [11]. Multiple births comprised 9% of the infertility group compared with 1.3% in the general population of Victoria, Australia, and 23.7% of IVF and GIFT births [12]. Thus, studies from all over the world have shown a very high rate of multiple births following IVF.

2.1. Problems associated with multiple births

Multiple pregnancy can pose a significant risk to both the mother and the baby, and is the single biggest health risk following IVF treatment. Women with multiple pregnancies have higher risks of miscarriage, anaemia, hypertensive disorders like pre-eclampsia, diabetes, operative deliveries and related postnatal illnesses. Although the mortality is low, morbidity figures are higher in these women than in women with singleton pregnancies. The risk of pre-eclampsia and gestational diabetes is 2–3 times higher in women with twins than in singleton pregnancies and 9 times higher with triplet pregnancy [13]. Advanced maternal age is a known risk factor and is associated with higher perinatal complications.

Several studies worldwide have reported that around 10% women with twins experience parenting stress, depression and marital problems [14]. In first-time mothers, twins with low birth weight have a particularly high impact on their personal, social and emotional wellbeing.

Most twins conceived as a result of IVF treatment happen to be dichorionic as a result of transfer of two or more embryos. Although the risk of chromosomal anomalies and cerebral palsy (CP) is seen more often in monochorionic twins, the risk of

prematurity and low birth weight is seen in both mono- and dichorionic twins equally. IVF twins are born approximately 3 weeks earlier than singletons and weigh 800–1000 gm less than their singleton counterparts [15].

The risk of CP increases from 1.7/1000 live births in singleton pregnancies to 6.2/1000 live births in twins [16]. Twins have at least a 6 times higher risk of developing CP and triplets have an 18 times higher risk. Most problems associated with twins appear to be related to prematurity and crucially the gestational age at birth. The risk of babies dying due to prematurity and low birth weight in the first month of life increases from 3 per 1000 for singletons to 19 per 1000 for multiple births. Low birth weight (<2500 gm), very low birth weight (<1500 gm) and extremely low birth weight (<1000 gm) are all mostly related to preterm deliveries in twins.

Three out of 4 babies born under 26 weeks' gestation are at risk of dying soon after birth or may require several months of care in the neonatal unit. Over 60% of survivors are likely to have significant brain and eye damage resulting in physical and mental impairment. These children end up having attention deficit hyperactive disorders and behavioural problems that are likely to persist into adult life [17].

Compared to singleton births, fetal, neonatal and perinatal mortality rates are 3–6 times higher in twins and 5–15 times in higher order multiple births in Australia [18]. CP rates among survivors are 6 times higher in twins and twenty times higher in triplets. In a study from Western Australia [19], the incidence of major birth defects was 7.1% in twins born after ART and 5.9% of non-ART twins of unlike sex. Studies by Venn and Lumley [12] showed that perinatal mortality between 1982 and 1990 was 11.1 per 1000 in general population and 34.9 per 1000 in the IVF group.

Thus, for nearly three decades problems due to multiple births have been identified, underlining the crucial fact that birth of a singleton term baby carries the optimum outcome for both mother and baby.

3. Strategies to reduce multiple births

The best way to reduce multiple births is to reduce the number of embryos transferred into the uterus. For the past two decades, the HFEA has encouraged clinics in the UK to take steps to reduce the risks of multiple births. In 1991, clinics were discouraged from transferring more than three embryos at one time in a treatment cycle. In 2001, the HFEA introduced a two-embryo transfer policy. In 2004, this was tightened further to allow a maximum of two embryos to be transferred in women under 40 years: for women aged 40 years and over, a maximum of three embryos could be transferred under exceptional circumstances. These early measures halved the number of triplet pregnancies in the UK but the twin pregnancy rate continued to rise. In 2007/2008, HFEA introduced an elective single embryo transfer (eSET) policy in a selected group of patients less than 37 years of age.

3.1. Acceptance of eSET so far

Based on national data, if 50% of women are offered and agree to eSET, the multiple birth rate would fall to less than 10%. In order to maintain the pregnancy rate using eSET, it is important to ensure that effective cryopreservation programmes are available to patients so that good quality embryos are available for another cycle.

The first study of single embryo transfer (SET) was conducted in Finland [20] and showed that pregnancy rates were not significantly different (14.7%) with SET and double embryo transfer (DET) in a specific population group. The rate of multiple births dropped to 5% in the SET group from 38% in the DET group. In 2003, Tiitinen et al. [21] reported a dramatic reduction in twin rates in

Download English Version:

<https://daneshyari.com/en/article/6174044>

Download Persian Version:

<https://daneshyari.com/article/6174044>

[Daneshyari.com](https://daneshyari.com)