Outcome in Clients with Positive Pregnancy Test Following IVF/ICSI Treatment

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Abstract

Background: A retrospective analysis of the outcome of all patients who have recorded a positive pregnancy test following IVF/ICSI treatment from June 1999 to December 2002 was done.

Materials and Methods: A total of 1256 treatment cycles were carried out using the long day 1 (early follicular phase) or day 21 (mid-luteal phase) protocol using gonadotrophins Menogon, Pergonal or Metrodin 150 300 IU for 12 to 15 days after pituitary down regulation with the GnRH analogue Buserelin.

Results: *A total of* 258 (20.5%) biochemical pregnancies were recorded. Sixty-seven (26%) resulted in early pregnancy loss (EPL) of which 10 (3.4%) were ectopic pregnancies. Clinical pregnancy occurred in the remaining 191 (74%) patients, with 20 (10.5%) resulting in miscarriages. A total of 160 babies (singletons/multiples) had been born by the end of the year 2002 with 40 ongoing pregnancies as at then.

Conclusion: Rate of early pregnancy loss in IVF/ICSI is not higher than in natural cycles and once clinical pregnancy is diagnosed, there is approximately a 90% chance of the pregnancy resulting in live birth, barring obstetric complications.

Key Words: In-vitro Fertilization (IVF), Intracytoplasmic Sperm Injection (ICSI), Outcome. [Trop J Obstet Gynaecol, 2005, 22: 9-11]

Introduction

Since the birth of first IVF child in 1978, the IVF procedure has become a common treatment for infertile couples, enabling them to have children. Later, ICSI was developed to enhance the results of male fertility treatment. Though a significant number of patients have benefited from Assisted Reproduction Technology (ART) techniques, the pregnancy rates are still not up to the patients' expectations. Increasing the pregnancy rates has always been a serious challenge in IVF.

The biological process of becoming pregnant is very complex. There is so much that has to go exactly right and so much that can go wrong. Embryo implantation rates in human IVF are low considering the number of embryos transferred compared to natural cycles and of course, to improve clinical outcome with this technology, there is need to focus on the mechanisms underlying implantation to enhance the chances of an embryo to implant[1]. Implantation comprises a series of events called apposition, adhesion and invasion that start when the blastocyst arrives in the endometrial cavity, approximately 6 to 7 days after ovulation. Nevertheless, in ART, implantation is clinically evaluated at days 14 to 16 after embryo transfer[2].

A rise in hCG concentration in either urine or serum has been used to detect the establishment of pregnancy within the first few weeks of conception. Failure to confirm the presence of embryonic sac(s) or fetal heart by subsequent ultrasound scan at 6 to 7 weeks gestation occurs in 18 to 22% of all pregnancies [3,4] and is sometimes described as early pregnancy loss (EPL), biochemical pregnancy or occult pregnancy[5]. The objective of this write-up is to analyze the outcome of all patients who have recorded a positive pregnancy test following IVF/ICSI treatment.

Materials and Methods

Retrospective analysis of 1256 IVF/ICSI treatment cycles carried out at The Bridge Clinic Limited from June 1999 to December 2002, in which patients had recorded a positive pregnancy test were considered. Ovarian stimulation was by the long protocol, with pituitary down regulation achieved with GnRH analogue, buserelin 0.5mls subcutaneous daily for 14 21 days and is confirmed by a transvaginal pre-FSH scan. It is expected that endometrial thickness is less than 4mm with absence of ovarian cysts greater than 10 mm diameter. Stimulation of superovulation is with Gonadotrophins (Pergonal or Menogon) or purified FSH (Metrodin) 150 300 IU for 12 to 15 days. Transvaginal ultrasound folliculogram (pre HCG scan) is done to assess number and sizes of follicles and to schedule patients for oocyte retrieval.

Conventional IVF or ICSI procedure was then done to generate embryos, which were transferred in to the uterus transcervically, 48 72 hours later. Blood pregnancy test is done 14 days after embryo transfer. First pregnancy scan is done one week after a positive

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pregnancy test to identify gestation sac(s) while a second pregnancy scan is done two weeks after to confirm clinical pregnancy through identification of fetal heartbeat. Patients are referred for ANC once clinical pregnancy is diagnosed. The outcome measures were biochemical pregnancy rate, early pregnancy loss (EPL) rate, clinical pregnancy rate, miscarriage rate and ectopic pregnancy rate.

Table 1

Early Pregnancy Data

Year	No of Treatment cycles	Biochemical Pregnancies (%)	Early Pregnancy Loss (EPL) (%)	Ectopic Pregnancy %	Clinical Pregnancy (%)
1999	109	18 (16.5)	4 (22.2)	—	14 (77.7)
2000	273	49 (17.9)	8 (16.3)	1	41 (83.7)
2001	448	95 (21.2)	25 (26.3)	5	70 (73.7)
2002	426	96 (22.5)	30 (30.2)	4	66 (68.8)
Total	1256	258 (20.5)	67 (26)	10 (3.4)	191 (74)

Results

109 treatment cycles were carried out in the year 1999, 18 biochemical pregnancies were recorded out of which 4 ended as early pregnancy loss and 14 clinical pregnancies were recorded giving 77.7 % of the total number of pregnancies. In the year 2000, 273 cycles were carried out, 49 (17.9%) biochemical pregnancies recorded, 8 EPL,1 ectopic and 41 clinical pregnancies recorded at 83.7% of total pregnancies. 448 cycles were done in 2001, with 95 pregnancies recorded, 25 lost as EPL, 5 ectopic pregnancies and 70 clinical pregnancies were recorded giving 73.7% of total pregnancies. In 2002, 426 cycles were done, 96 pregnancies recorded, out of which 30 (30.2%) ended as EPL, 4 ectopics and 66 clinical pregnancies (68.8%) recorded. In total, during the period under review, treatment cycles were undertaken, 258 biochemical pregnancies were recorded, 67 (26%) ended as EPL, 10 (3.4%) as ectopics and 191 (74%) as clinical pregnancies. (Table 1)

The 14 clinical pregnancies recorded in 1999 progressed into live births while in year 2000, 41 clinical pregnancies with 6 miscarriages and 35 live births were recorded. 70 pregnancies recorded in 2001, with 7 miscarriages and 35 live births. In 2002, 66 clinical pregnancies, with 7 miscarriages and 75 live births were obtained. In all, between 1999 and 2002, there were 191 clinical pregnancies, 20 miscarriages (10.5%) and 136 live births with 40 on-going pregnancies as at the end of 2002 (Table 2).

Table 2

Early Pregnancy Data

Year	No of Clinical Pregnancies	No of Miscariages	No of Live-births	On-going pregnancies
1999	14	—	—	14
2000	41	6	35	25
2001	70	7	36	29
2002	66	7	75	40
Total	191	20 (10.5%)	136	

Discussion

Our centre started operations in mid-1999 with the collaboration of IVF specialists from the U.K. At the onset, treatment was carried out in batches and this continued till the end of 2000, when a wholly Nigerian team took over. This may have accounted for the sharp increase in no of patients treated between 2000 and 2001 as treatment now became readily available, coupled with the increased awareness of IVF as a viable treatment modality for infertility. The pregnancy rate/ treatment cycle also show a little increase from what was obtained at the beginning as proficiency increases in the handling of the 'high tech' equipments involved in ART. As a result, biochemical pregnancy rate/treatment cycle at the end of year 2002 compare favourably with what obtains elsewhere [6].

The early pregnancy loss (EPL) rate recorded is within the limits of what happens in the natural setting showing that IVF is not in any way associated with increased pregnancy loss contrary to belief in certain quarters [2,7]. Although the practice of multiple embryo transfer in ART also means that some EPL may be hidden by the continuing growth of companion embryo(s). It is therefore likely that the real risk of EPL may be higher in ART population than in the general population although direct evidence to support this assertion is yet to be obtained[8]. Although we could not investigate the mechanism of EPL in our center, it has been suggested that EPL may be due to failure of the maternal support system or through the impairment of the fetus itself. Due to the extreme difficulty in obtaining pregnancy material in EPL, the determination of either a pathological or a chromosomal cause is hard.

Ectopic pregnancy is a pregnancy complication that is also important in IVF practice. In actual fact, the world's first IVF pregnancy in 1996 ended up in the woman's fallopian tube instead of her uterus. Even though the embryos are placed in the uterus, they may drift into a fallopian tube. Ectopic pregnancy rate in our centre of 3.44% compares favourably with findings from other centers [9,10]. Success rate in IVF treatment have so far been fairly constant at around 25% until the age of 34 years when there is a steep decline [11]. This success rate sounds good enough considering the fact that the clients that come for IVF are supposedly the 'bad cases'. These are people who cannot get pregnant on their own and still fail to get pregnant by routine infertility treatment, so in effect they have been 'doubly selected' out of the normal population.

However, for the about three-quarters of patients with negative outcome, it's a very distressing situation having gone through the financial and heavy psychological costs of the procedure [12]. Can we bring happiness to more couples? Or can we have better predictors of the outcome, to save those unfortunate couples from going through the heavy burden of the procedure if they have no chance of success. These are part of the challenges facing ART practitioners for which extensive research is on going.

Our centre has from onset focused on ART. Hence patients who achieved clinical pregnancies are referred back to their doctors for antenatal care. The patients' progresses are however followed up and the outcomes of their pregnancies are documented. The outcome of course, is subject to the quality of antenatal care received at the referral clinics. The fact that the technology of ART could be successfully transferred to sub-saharan Africa is no longer in doubt judging from the successes so far recorded by the pioneer IVF centres and also, by the fact that it is a rapidly expanding field even in Nigeria, which now has about a dozen centres located mainly in the urban cities of Lagos, Port-Harcourt and Abuja. There is an urgent need for the development of appropriate regulations and guidelines on ART as is the case in the developed countries and ART practitioners should have collaborative meetings and share their statistics and expertise.

References

1. Simon C, Moreno C, Remohi J, Pellicer A. Molecular interactions between embryo and uterus in the adhesion phase of human implantation. *Hum Reprod*, 1998; 13: 101104.
2. Simon C, Landeras J, Zuzuarreui J, Martin JC, Remohi J, Pellicer A. Early pregnancy losses in IVF and oocyte donation. *Fertil Steril*, 1999, 2(6): 10611065.
3. Alfredsson J. Incidence of spontaneous abortion following artificial insemination by donor. *Int J Fertil*, 1998, 33: 241245.
4. Wilcox AJ, Weinberg CR, O'Connor JF, *et al.* Incidence of early pregnancy loss. *N Engl J Med*, 1988; 319: 189194.
5. Zinaman MJ, Clegg ED, Brown CC, et al. Estimates of human fertility and pregnancy loss. *Fertil Steril*, 1996; 65: 503509.
6. Giwa-Osagie O. F. ART in developing countries with particular reference to sub-saharan Africa. In: Vayena, P. Rowe, P Griffin (eds), *Report of a Meeting on Medical, Ethical and Social Aspects of Assisted Reproduction*. Geneva: WHO, 2001; 2227.
7. Steer C, Campbell S, Davies M, Collins W. *Spontaneous abortion rates after natural and assisted conception. Br Med J*, 1989; 299: 13171318.
8. Winter E, Wang J, Davies M. J, Norman R. Early pregnancy loss following assisted reproductive treatment. *Hum Reprod*, 2002; 17(12): 32203223.
9. Karande V, C, Flood J. T, Heard N. et al Analysis of ectopic pregnancies resulting from in vitro fertilization and embryo transfer. *Hum Reprod*, 1991; 446449.
10. Roest J, Mons HV, Zeilmaker GH, Verhoef A. The incidence of major clinical complications ia a Dutch transport IVF programme. *Hum Reprod* (Update), (1996); 2(4): 345353.
11. Society for Assisted Reproductive Technology and The American Society for Reproductive Medicine, Assisted Reproductive Technology in the United States and Canada: 1995 results generated from the Registry. *Fertil Steril*, 1998; 69: 389398.
12. Mahmoud F. Fathalla. Current Challenges in Assisted Reproduction. In: Vayena, P. Rowe, P Griffin (eds), *Report of a meeting on Medical, Ethical and Social Aspects of Assisted Reproduction*. Geneva: WHO, 2001; 3-12.