

Maternal and Fetal Outcomes in Pregnancies Conceived with In-Vitro Fertilization

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ABSTRACT:

Objective: To assess the outcome of pregnancies conceived by in vitro fertilization.

Materials and Methods: A retrospective study utilizing case notes of 110 cases of in vitro fertilization (IVF) delivered in East Sussex Hospital Trust (ESHT) was carried out from 2010 to 2011 in two district general hospitals, Eastbourne and Conquest hospital that come under ESHT. All cases with IVF during these two years were included. Demographic details, predisposing risk factors, body mass index, causes of infertility, antenatal care, onset of labour, mode of delivery and details of baby were collected and analysed.

Results: Infertility was female related in 46% and male related in 38%. In females tubal factor was the main cause. 18% had pre-existing medical conditions, polycystic ovaries being the commonest. 75% had singleton pregnancy and 25% twin's. Nearly 6% had antepartum haemorrhage, twins having higher (11%) rates compared to singleton pregnancy (3.6%). The incidence of pregnancy induced hypertension and diabetes were the same being more in twin compared to singleton pregnancy. There were 8.4% singleton preterm deliveries. The singleton babies born with weight of less than 2500 gms were 4.8%. There were 2 (1.8%) stillbirths. 3.6% babies had congenital abnormality. In 42 % mode of delivery was caesarean section.

Conclusion: Majority of children born following IVF had a good outcome but increased risk of obstetrics and fetal complications was found when compared to spontaneously conceived pregnancies. Multiple births remain a major cause of morbidity among infertility patients

Keywords: Infertility, Assisted reproduction, In vitro fertilization, Maternal outcome, Fetal outcome.

INTRODUCTION:

It is estimated that infertility affects 15-20% of the couples in the UK at some stage in their reproductive life.^{1,2} Assisted reproduction techniques have developed to improve chances of achieving pregnancy in subfertile couples. Assisted reproduction techniques have subsequently become an effective and widely used therapy for such couples. In vitro fertilisation (IVF) is one of these techniques. Most (80 %) of the sub fertile couples conceive with assisted reproductive technology

(ART), but still 20% will not be able to conceive³. In women aged 40 years treatment of infertility is difficult and controversial⁴. Reasons for the increasing infertility are delaying the childbearing, increased pelvic infections and deteriorating sperm quality⁵. The reasons for infertility are related to both females and males. The most common causes for infertility are ovulatory disorder or anovulation, tubal factor, endometriosis, abnormal semen parameters. Infertility in many couples can have multiple causes. In about 15-17% of couples, no reason for infertility is found.⁶ IVF is the treatment of choice for infertility that has not been successfully treated by other modalities.^{5,7,8} Most of the pregnancies after IVF have good outcomes, but there is also an increased risk of obstetric and neonatal complications, compared to naturally conceived pregnancies⁹. Pregnancies from IVF has increased risk of perinatal mortality, congenital anomalies and is associated with higher rates of preterm deliveries, prematurity, antepartum haemorrhage, caesarean sections, fetal malpresentation, small for gestational age, low birth weight and admission to neonatal intensive care unit. The risk of pregnancy-induced hypertension, pre-eclampsia, placenta previa and non-insulin-dependent gestational diabetes increases in IVF-pregnancies as well.^{10,11,12,13} It is not clear whether these increased risks are related to infertility, or use of assisted reproductive techniques¹⁴. The causes of infertility influence the outcome of ART treatment. The prognosis with unexplained infertility is better than tubal infertility or endometriosis. The duration of infertility and parity of women also have influence on pregnancy rates achieved by ART. An increase in duration of infertility will decrease the chance of successful IVF treatment.¹⁵ A previous pregnancy and delivery with IVF treatment, increases the chance of success in a subsequent IVF treatment¹⁶. Couples with secondary infertility have double pregnancy rates compared to primary infertility.¹⁷

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¹⁸ There is significant risk of multiple pregnancies with ART. The rate of multiple pregnancies being approximately 25-35%^{19,20} compared with only 1% in naturally conceived pregnancies. Multiple pregnancies increase the risk of foetal and maternal complications. The Dichorionic twins are most common, but the incidence of monochorionic twins is also increasing¹⁴. In vitro fertilization increases the risk of monozygotic twins by two folds compared with natural conception. Malformation rates in IVF multiple pregnancies are higher than in IVF singletons^{21,22}. Multiple births are a leading cause of long-term child morbidity among infertility couples.²³(Table 1). Present study was undertaken to assess the outcome of pregnancies conceived by in vitro fertilization.

MATERIALS AND METHODS:

This retrospective study utilizing case notes of 110 cases of in vitro fertilization (IVF) delivered in East Sussex Hospital Trust (ESHT) was carried out from 2010 to 2011 in two district general hospitals, Eastbourne and Conquest hospital that come under ESHT. All cases with IVF during these two years were included. Demographic details, predisposing risk factors, body mass index, causes of infertility, antenatal care, onset of labour, mode of delivery and details of baby were collected and analysed.

RESULTS:

110 cases were studied. Most of these pregnancies had consultant lead care except 4 cases which had only midwifery care. Those who had assisted reproduction with primary infertility were 68 %. About 35% who had treatment were of ages 31-35 years and 29% were aged 36-40 year. 40.9% had BMI 25-30 and 5.46% had BMI 31 and above (Table 2). In 46% subfertility was female related and 38% cases male related. In females 23% tubal factor and 13% endometriosis were responsible. In 13% cases cause was unexplained and in 7.2% there were more than one cause of infertility. 18% had pre-existing medical condition, the incidence of polycystic ovaries were 75% (Table 3). In our study 75% had singleton pregnancy and 25% twins. Those who suffered from pregnancy induced hypertension (PIH) were around 5%. Singleton 4% and 8% twin pregnancy suffered from pregnancy induced hypertension. The numbers of patients with diabetes were the same as PIH (5%) and the distribution were the same as in PIH, about 4% in singleton and 8% in twins. There was antepartum haemorrhage in nearly 6% of cases. It occurred in about 4% in singleton and 11% in twin pregnancy. There were 16% cases which had no scan in the third trimester. There were 8.4% singleton preterm deliveries and 15% twin pregnancy. The singleton babies born with weight of less than 2500gms were 4.8%. There were 1.8% stillbirths, one singleton at 41+ weeks and one DCDA twin at 33 weeks. About 3.6%

babies had congenital abnormalities. Induction of labour was done in 33% of the cases. In 42% , mode of delivery were spontaneous vaginal ,16% had instrumental deliveries and around 42% were delivered by caesarean section There were 59% emergency and 41% elective caesarean sections (Table 4) .

Table: 1
Comparison of IVF & natural conception outcomes RCOG data

	IVF pregnancy	Natural Conception	Comments
Miscarriage	14-30%	15-20%	Slight increase, due to older age.
Ectopic pregnancy	1-11%	0.2-1.4%	Increase due to many factors
Preterm delivery	24-30%	6-7%	Four-fold increase.
Small birth weight	27-32%	5-7%	Five-fold increase.
Stillbirth rate	1.2%	0.6%	Two-fold increase.
Perinatal death	2.7%	1.0%	Two-fold to four-fold increased risk.
Congenital abnormalities	1.0-5.4%	0.8-4.5%	30-40% increase. However, the absolute risk is nevertheless low. The increase is partly attributable to the underlying infertility as couples who take longer than 12 months to conceive also have an increased risk of abnormalities.
Caesarean section	33-58%	10-25%	Increase mainly because of multiple pregnancy and woman's age.
Multiple pregnancy			
twins	24-31%	1.2-4.5%	Increase due to higher number of embryos transferred.
triplets	0.5-5.2%	0.012%	
quadruplets	0.5%	0.0001%	

Table: 2
N=110

Parameter	IVF Pregnancy	Percentage (%)
Age in years	31-35	35%
	36-40	29%
BMI	25-30	40.9%
	31 & above	5.46%

Table: 3
N=110
Causes of Infertility

Causes	Percentage (%)
Tubal factor	23%
Endometriosis	13%
polycystic ovaries	75%.
Unexplained	13%
More than 1 cause	7.2%

Table: 4
N=110
Pregnancy Outcomes

Outcome	Percentage (%)
PIH	5%
Gestational Diabetes	5%
APH	6%
Preterm delivery	8%
Induction of labor	33%
Mode of Delivery	
Spontaneous vaginal	42%
Instrumental	16%
Caesarean section	42%
(i) Emergency	59%
(ii) Elective	41%
Baby weight	
Less than 2500 gm	4.8%
Still births	1.8%
Congenital Abnormalities	3.6%

DISCUSSION:

The findings of our study showed that maternal, obstetric and foetal complications increase in IVF pregnancies. In our study 75% had singleton pregnancy and 25% twins which is comparable to the United Kingdom (HFEA patient's guide 2002), 25% of deliveries after IVF were twins. The stillbirth rate in our study is 1.8% compared to 0.6% in naturally conceived pregnancy. Two fold increase risk in stillbirth by IVF has been reported but in our study threefold increase was noted compared to naturally conceived pregnancies. There is two-fold to four-fold increased risk of perinatal death with IVF pregnancy compared to spontaneously conceived pregnancy²⁴ however there was no perinatal death in our study. The incidence of pregnancy induced hypertension and diabetes were the same in IVF pregnancies. It is concerning that the incidence was twice in twins as compared to singleton pregnancy. This study also confirmed that polycystic ovaries have a significant role in infertility. The preterm delivery of singleton pregnancy with IVF is 12-14%, our study showed 8.4% compared to 6-7 % in naturally conceived. This study also confirmed increased risk of preterm delivery compared to naturally conceived pregnancy. However the risk of preterm delivery is increased two fold in twins. Babies who had congenital abnormalities were 3.6%, whereas in naturally conceived pregnancy it is 0.8- 4.5%. However the absolute risk is low. The increase in congenital abnormality may be partly attributable to the underlying infertility. There are evidences that couples who took longer than 12 months to conceive have an increased risk of structural chromosomal abnormalities. The IVF techniques themselves could be involved. Another possible cause is that babies conceived through fertility treatments are monitored more closely than other babies We found an increased risk of Caesarean sections with IVF pregnancy, 42% compared to 10-25% naturally conceived pregnancy. The increased risk can be because of maternal age and the risks associated with IVF pregnancy.²⁵ The success of assisted reproductive technology should not only be in terms of live birth rates, but also in terms of reduction of multiple births to singleton babies. Efforts should be made to limit multiple pregnancies resulting from ART. Women receiving in vitro fertilisation should be counselled about the increase obstetrical risks and interventions. They need to be made aware of psychosocial implications of assisted conception techniques. Clear information in different languages of choice and patient information leaflets should be available. Close surveillance during pregnancy is required in pregnancies conceived with IVF. Evidence from randomized controlled trials, have shown significant reduction in the probability of live birth and multiple birth, when comparing double embryo transfer with single embryo transfer. These trials suggests that increasing the number of attempts of single embryo transfer results in a cumulative live birth rate similar to that of two embryo transfer. The live birth from single embryo has less complications as well financial burden than two embryo transfer²⁶ Our study confirmed that

maternal, obstetric and foetal complications increase in IVF pregnancies as seen by many other studies in literature.^{27,28,29} This study also showed that multiple pregnancies is the most powerful predictive factor for adverse maternal, obstetrical, and perinatal outcomes as concluded by many other studies²³.

The limitations of our study are, our model was based on data from a single centre .It was a retrospective study, our analysis depended on previously recorded data from the notes, therefore some data was missing. We did not have comparable data from the same trust on women of the same age who conceived naturally regarding maternal background such as body mass index, medical complications and mode of delivery .Other limitation was the sample size and the ethnicity. This study was conducted mainly on Caucasians so there was no ethnic diversity. There were however some inconsistencies in relation to management of IVF pregnancies, particularly in relation to singleton pregnancies .Some women were not assessed in consultant clinics .There was no agreement on timing of birth. All the women did not have the regular growth scans in third trimester .In the future there should be a reduction of the multiple pregnancies and a higher rate of singletons after adoption of a single embryo transfer policy. This will reduce the cost of the trust in providing care for these pregnancies. Trusts should have regular review and audits on the management effectiveness of in vitro conceived pregnancies. The increased rate of congenital abnormalities may be due to the fact that children conceived with artificial reproduction techniques have more vigilant follow up as compared to general populations. The strengths of the study are that majority of the women had treatment for primary infertility and had good outcome. We also found that data was comparable to national level for demographic and pregnancy outcome with IVF pregnancy.

CONCLUSION:

Majority of children born following IVF had a good outcome but increased risk of obstetrics and fetal complications was found when compared to spontaneously conceived pregnancies. Multiple births remain a major cause of morbidity among infertility patients. It is recommended that there should be a policy of trust for the management of IVF/ICSI singleton pregnancies, to improve compliance to recognised standards; ensuring community midwives refer IVF pregnancies for consultant-led antenatal care. These pregnancies should have at least two third trimester growth scans due to high risk nature of IVF pregnancies There is need to develop consensus agreement regarding timing of birth for singleton IVF babies.

Further research is required to determine the cause and increased risks to children as well as cancer associated with artificial reproduction technique. There is no research on the long-term health outcomes in women and children after IVF .This is because of the confidentiality affected by Human Fertilization and Embryology Act in the United Kingdom to the parents

and children resulted from ART has meant that follow up of these children has not been possible.

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