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Original Research Article

Outcome of singleton pregnancy following in-vitro fertilization: a prospective study

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ABSTRACT

Background: It is observed that any spontaneous pregnancy does not always result in healthy baby and healthy mother. The aim of the study was to study the obstetrical outcome of singleton pregnancies following in vitro fertilization and embryo transfer (IVF-ET).
Methods: All cases undergoing IVF-ET at ART Centre were followed up after Day18 (of ET) for estimation of serum beta HCG and trans-vaginal ultrasound done on day 21 and 5th week. The selected singleton pregnancies were followed for the various parameters to be studied and the data was statistically analyzed. A resultant 73 patients with single intrauterine gestational sac was followed up.
Results: In our study population of 73 post IVF-ET singleton pregnancies, 13.69% underwent first and second trimester abortions. They had increased risk of developing hypertensive disorders in pregnancy. Study also showed increased incidence of gestational diabetes mellitus. Yet another important outcome also included pregnancy with intrauterine growth restriction. Preterm birth was noted in 10 singleton pregnancies. Out of 73 followed up patients one third underwent caesarean delivery and another few underwent instrumental delivery. One in four babies accounted for weight more than 2.5 kgs. Out of followed up 73 cases of singleton IVF-ET pregnancies, 5 cases had congenital anomalies. Most common indication for NICU admission was respiratory distress. The incidence of small for gestational age came out to be significant.
Conclusions: Outcome of singleton pregnancy after IVF-ET is associated with adverse pregnancy outcomes. Couples should be made aware that even singleton pregnancies resulting from ART are at increased risk for obstetric complications.

Keywords: Embryo transfer, In vitro fertilization, NICU, Preterm birth, Singleton pregnancy

INTRODUCTION

The team of Dr Patrick Steptoe, the gynaecologist and Robert G Edwards, the physiologist carried out normal cycle In Vitro Fertilization resulting in the birth of the first test tube baby of the world – Louise Joy Brown on July 25th 1978 and laid the foundation of Assisted Reproductive Technologies (ART).[1]

In vitro fertilization (IVF) is a process by which the ovum (female gamete) and the sperm (male gamete) are fertilized and cleaved in the controlled laboratory conditions. Over the years since 1978 till date lot many advances have occurred to improve the results and outcome of the IVF pregnancies. This includes Controlled Ovarian Hyperstimulation (COH) using gonadotropins, the various sperm retrieval techniques like TESA (Testicular Sperm Aspiration), TESE (Testicular

sperm extraction), MESA (Microsurgical Epididymal Sperm Aspiration), and PESA (Percutaneous Epididymal Sperm Aspiration). The IVF procedure can be a conventional IVF, IVF with Intra Cytoplasmic Sperm Injection (ICSI) and also IVF with Intracytoplasmic Morphologically Selected Sperm Injection (IMSI). The number of embryo transferred (1, 2 or 3) and the day on which they are transferred (D2, D3 or D5), all these factors effect the implantation rate in the ART procedure.[2,3]

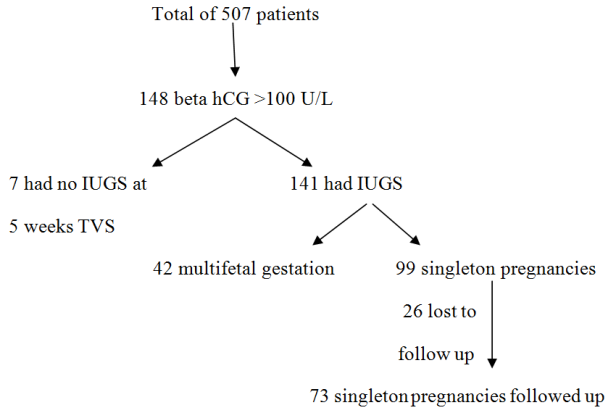
The development of Spindle View System and Embryoscope (to visualise dynamic growth and selection of embryo) and hatching of embryo (mechanical or laser) have helped to improve implantation rates and outcome of pregnancy.[4] Depending upon the number of embryos transferred the patient gets singleton, twin or higher order pregnancy. The incidence of uniovular twinning remains constant whereas twinning in higher order pregnancy depends upon the higher number of embryos transferred and successful implantation rate. It is observed that any spontaneous pregnancy does not result in healthy baby and healthy mother. Whether the singleton pregnancies resulting from IVF-ET would have the same outcome or different is the subject of my study.

METHODS

The study was conducted at ART Centre in Department of Obstetrics and Gynaecology, a tertiary care teaching hospital Pune. All patients of ART Centre, who would undergo IVF-ET and would carry a singleton babies were included in the study. All cases of twin or higher order IVF-ET pregnancy and frozen embryo transfer were excluded from the study. After exclusion, 74 cases of singleton pregnancy resulting from IVF-ET were followed up for the study. It was a 2 years study from Oct 2013 to June 2015. Ethical clearance was obtained from institutional ethics committee of the medical college where the author is affiliated.

All cases were followed up after Day18 (of ET) for estimation of serum beta HCG and transvaginal ultrasound done on day 21 and 5th week. If the scan showed single intrauterine sac with single fetal cardiac activity at 5th week, the pregnancy was followed up. If the scan suggested multiple sac or two or more foetal cardiac activity, that pregnancy was excluded from the study. The selected singleton pregnancies were followed for the various parameters to be studied and the data was statistically analysed.

In this study, outcome of 507 patients were followed up, who underwent IVF-ET at ART Centre in the given study period. Out of these 507 patients, 148 had serum beta hCG more than 100 IU/L. 99 had SIUGS at 5th week transvaginal ultrasound. 7 cases had no intrauterine gestational sac, out of which 4 turned out to be ectopic, which was managed accordingly. 42 cases turned out to be twin gestation, thus were excluded from the study. 26 cases were lost to follow up (they selected other centres for further follow up).Thus a resultant 73 patients with single intrauterine gestational sac was followed up.



RESULTS

Table 1: Maternal outcome in singleton pregnancy resulting from IVF-ET.

Outcomes		No. of cases	%
Ectopic pregnancy		04/148	2.70
Missed abortion		07/73	9.68
IUGR		07/73	9.68
IUFD		01/73	1.38
Preterm delivery	34-37 wks	07/73	13.69
	31-34 wks	0/73	
	<31 wks	03/73	
Mode of delivery	Normal vaginal	38/73	52.50
	Vacuum	05/73	08.54
	Caesarean	20/73	27.38

Table 2: Neonatal outcomes in singleton pregnancy resulting from IVF-ET.

Outcome	No. of cases	%
Low birth weight	14/63	22.22
Small for gestational age	06/63	09.52
Congenital anomalies	05/73	08.84
NICU admission	11/63	17.48

Out of the 73 cases of singleton pregnancies resulting from IVF-ET, majority belong to the age group of 26-30 years (52.05%), and second majority in the age group of 31-35 (27.39%). The mean age of women in this study is 28.76 years. Most of the patients, who carried singleton pregnancy after IVF-ET, were cases of primary infertility (78.08%). After ovum pick up, embryo transfer was performed on D2, D3 OR D5. Out of resultant 73 singleton pregnancies following IVF-ET in our study population, 82.19% had undergone ET on D2 followed by 13.69 % in D3. In our study population of 67 singleton pregnancies, 53.42% had underwent double embryo transfer, whereas 35.62% had underwent triple embryo transfer.

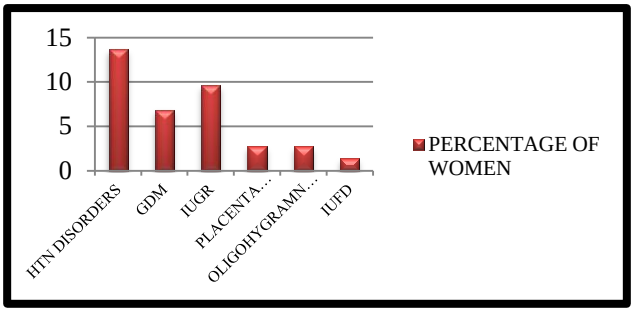


Figure 2: Antenatal complication in women with singleton post IVF-ET pregnancy.

With a beta hCG of >100 U/L, 148 patients underwent TVS on day 21 And again on 5th week POG. Out of 148 patients, 141 had intrauterine gestational sac, whereas 07 patients (04.72%) had no intrauterine gestational sac and were labelled as pregnancy of unknown location (PUL). In our study population of 67 post IVF-ET singleton pregnancies, 13.69% underwent first and second trimester abortions. Out of these, 4.10% were spontaneous first trimester losses, whereas 2.73% were second trimester fetal losses. The net percentage of 09.58% accounted for missed abortions.

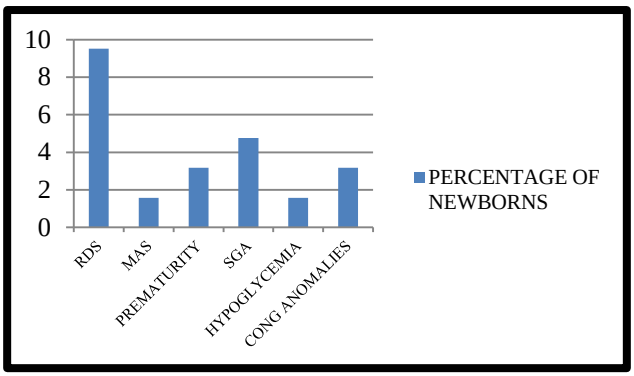


Figure 3: Indications of NICU admission in neonates of singleton post IVF-ET pregnancy.

On antenatal follow up of our study population, 13.69% developed hypertensive disorders in pregnancy (Figure 1). Another 6.84% had gestational diabetes mellitus. Yet another important outcome also included pregnancy with intrauterine growth restriction (9.58%). One case of IUFD was also noted. 72.60% of followed singletons delivered at or after 37 weeks of gestation. Preterm birth was noted in 10 (13.69%) singleton pregnancies. Out of 73 followed up patients, 27.38% underwent caesarean delivery and another 6.84% underwent instrumental delivery. Out of 63 patients who delivered either term or preterm; 22.22% babies were low birth weight. Only 77.78% babies accounted for weight more than 2.5 kgs.

Out of followed up 73 cases of singleton IVF-ET pregnancies, 5 cases had congenital anomalies (06.84%). Out of 57 babies delivered, 17.46% were admitted in NICU for various indications. Most common indication for NICU admission (Figure 2) was respiratory distress (9.52%). Other causes included meconium aspiration (1.58%); small for gestational age (4.76%); prematurity (3.17%) and congenital anomalies (3.17%). There was 1 case (1.58%) of neonatal mortality due to severe prematurity with respiratory distress syndrome. The incidence of small for gestational age came out to be 09.52%.

DISCUSSION

Strandell et al have shown tubal factor infertility to be one of the risk factors for ectopic pregnancy after IVF. The incidence of IVF ectopic pregnancy ranges from 1.8-11% among those with tubal factor infertility. Thus the exact incidence of ectopic after IVF reasonably depends on the cause of infertility the patient was having. In the results generated by ASRM in 2007, there were 560 ectopic pregnancies, representing 1.8% of all pregnancies following IVF. The Canadian ART registry 2009 reported 51 cases of ectopic pregnancies among 2499 clinical pregnancies (2.04%) after IVF/ICSI treatment.[5] In our study the rates of ectopic pregnancy were 2.7%. In a prospective study done by Mohammed Malak et al, Montreal on 365 women who conceived after IVF-ET, 18 (4.9%) had ectopic pregnancy.[6]

The clinical abortion rate of IVF patients (25%) has been reported to be higher than that of naturally conception (15%).[7] In our study 10 out of 73 (13.69%) singleton pregnancies underwent first and second trimester abortion. Of which first trimester losses included 8 (10.95%) cases. This is in match with the abortion rates after natural conception.

In our study intra uterine growth restriction detected antenatally was 7 in 73 (9.58%) cases. This was in correspondence with the study done by Jackson RA et al in 2004 regarding perinatal outcomes in IVF pregnancies (9.5%).[8] In our study there was one case of intrauterine foetal death at 30 weeks period of gestation (1.36%). According to Jackson R A et al, the incidence of still birth in their study was 1.2%.[8] The incidence of still born in these subset of population is higher than that of normal population.

Preterm birth in IVF pregnancies has been studied extensively. Earlier multifetal gestation following IVF was thought to be the factor causing preterm delivery. But later in 1985 it was studied that singleton pregnancies also result in preterm birth. In our study there were 10 (13.69%) preterm births. Out of these 10 cases, (4%) were extreme preterm (<31 weeks). According to the Dutch study by Koudstaal and Braat et al, the incidence of preterm birth was 15%. According to the study done by Jackson R A etal the incidence was 11.5%.[8]

In our study the rate of cesarean section was 27.38% (20 among 73 singleton pregnancies). Out of this, 11 (15%) were emergency cesarean done after a trial for normal vaginal delivery. These rates of cesarean sections are comparable to those in normal population. In the Dutch study by Koudstaal et al, the incidence of cesarean

delivery was just 16%.[9] They concluded that there was no additional increase in cesarean rates due to singleton post IVF-ET pregnancies.

The incidence of birth weight less than 2500 g in the Dutch study was 13%. This is significantly more than that in singleton pregnancies after normal conception (7%) in Dutch population. In the study by Jackson R A et al, 2004, the incidence of low birth weight was 12%.[8] The incidence of low birth weight in our study is 22%. This is mainly due to following reasons. One is increased number of preterm deliveries in this group, both induced and spontaneous. Secondly, the Indian growth pattern differs from that of western growth. The incidence of low birth weight in India is 18%. Thus a high rate of low birth weight signifies the importance of neonatal care required.

Congenital anomalies have been mentioned in literature as an adverse event associated with IVF pregnancies. These are increased in context to multiple gestations after IVF-ET. But it is now clear that singleton pregnancies following IVF-ET also carry the risk of congenital anomalies. The most common mentioned anomalies are hypospadiasis, neural tube defects and congenital heart disease. In our study, 5 among 73 IVF singleton pregnancies (6.84%) had congenital anomalies. This was in coherence with the study by Klemetti R and Gissler et al, 2005 which mentions incidence of 5.8%.[10]

In our study a total of 11 among 63 new-borns (17.46%) were admitted in NICU for multiple reasons. The most common reason for admission being respiratory distress associated with prematurity. According to the study of perinatal outcomes in singleton assisted pregnancies published in BMJ, the incidence is 14%. The study by Jackson R A et al in 2004 also suggests an incidence of 17.8%.[8] The incidence of these babies going for neonatal intensive care is high because of prematurity leading to respiratory distress and low birth weight which are the primary reasons for admissions to NICU. There were few shortcomings in this study. This was just an observational study and sample size was small. Maternal comorbidities like advanced maternal age, hypertension, diabetes mellitus, which can influence the results of the study, were not excluded. Also long term follow up of neonate was not done.

CONCLUSION

Couples should be made aware that even singleton pregnancies resulting from ART are at increased risk for obstetric complications, including preterm birth and small for gestational age infants, compared to spontaneously conceived gestations. The observed frequency of adverse outcomes should be described and comparison with frequencies in spontaneous conceptions may be discussed. It is not possible, at this time, to quantify for patients the separate contributions of the ART procedures and the underlying fertility disorder to the excess risk, nor does sufficient evidence exist to allow a differential estimate of perinatal risks by specific treatment or etiology of infertility. Similarly, no specific data exist on which clinicians caring for women with ART pregnancies can base recommendations for any particular antenatal monitoring for or effective preventive measures against these outcomes, beyond current standard obstetrical practice.

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