

# Is Safe Maternal Outcome Of IVF Pregnancies Our Future?

<sup>1</sup>Nosheen Rashid; <sup>2</sup>Shaila Banu

<sup>1</sup>Nosheen Rashid, Senior clinical Fellow, obstetrics and gynecology, Wexham Park Hospital, Slough, UK

<sup>2</sup>Shaila Banu, Post CCT specialty Doctor, obstetrics and gynecology, Wexham Park Hospital, Slough, UK

## Abstract:

### Introduction:

Infertility affects about 1 in 7 couples in UK and around 1% of them seek in vitro fertilization (IVF) treatment for conception every year. IVF is associated with adverse maternal and perinatal outcome although majority of these pregnancies remain uncomplicated with optimum outcome.

### Objective:

The main objective of our study was to look into outcome of pregnancies in women conceived through IVF treatment in order to evaluate our maternity care and identify areas requiring improvement.

### Materials and Methods:

A retrospective study of patients' hand held maternity notes supplemented by information obtained from electronic record of patient care for each trimester of pregnancy and labour was completed in Wexham Park Hospital, Frimley Health NHS Trust in 2017. Total of 62 patients were recruited, among them data was collected from 40 patients due to incomplete or missing information in the remaining patients. Data was analysed by Trust audit department.

### Results:

In our study, 80% of women were either from white British or Asian background. Among them, 72% were between 30 – 40 years of age and around 70% had BMI between 20-30. In Index pregnancy, 5% of pregnancies in first trimester ended in spontaneous miscarriages. Booking blood pressure was within normal range in all but one woman who entered into pregnancy with chronic hypertension controlled with labetalol. 70% of pregnant women were advised to start aspirin at their 12 weeks review by obstetrician in hospital antenatal clinic based on individual thromboembolic risks in pregnancy. Combined screening tests were normal in more than 90% of cases. In 8% pregnancies congenital fetal abnormalities were detected. Glucose tolerant test was positive in 30% of women, 20% among them had their gestational diabetes controlled with diet only, 5% required metformin and 5% of women had insulin in addition to metformin. Around 23% of women delivered before 37 weeks of pregnancy, 5% of them delivered before 32 weeks of gestation. Approximately 57% required delivery by Caesarean section, 30% as emergency and 27% were elective procedures.

**Conclusion:** IVF pregnancy is recognised as a high-risk pregnancy and is associated with adverse obstetric outcome. Our study suggests that through robust risk assessment process at booking and provision of appropriate gestation based care, optimum maternal and perinatal outcome can be achieved.

**Keywords:** Subfertility, Artificial reproductive technology (ART), In vitro fertilization (IVF), Intrauterine growth restriction (IUGR), Dichorionic diamniotic twin (DCDA), Small for gestational age (SGA), Gestational diabetes mellitus (GDM)

## INTRODUCTION:

Subfertility is defined as inability to conceive after one year of regular unprotected sexual intercourse. Delaying conception by couple for a variety of reasons has been recognized as a factor for subfertility. Around 1 in 8 couples have trouble in conceiving or sustaining a pregnancy[1]. In vitro fertilization (IVF) is the biggest breakthrough of this century. IVF involves ovarian stimulation with gonadotropin hormones, followed by retrieval of oocytes under sedation with subsequent fertilization by sperm in the laboratory, and development of embryos in culture prior to transfer into the uterus. IVF can be done by using native or donor oocyte[2]. IVF pregnancy is a high risk pregnancy, although majority of them have satisfactory obstetric outcome. In UK law, every couple seeking IVF treatment should be counseled of the risks such as ovarian hyper stimulation syndrome which is unique to infertility treatment. IVF pregnancies may have adverse maternal and perinatal outcome such as pregnancy induced hypertension, pre-eclampsia, gestational diabetes mellitus, post-partum haemorrhage, intrauterine growth restriction, preterm labour[3,4]. Increased obstetric risks may account for the high incidence of poor obstetric outcome, e.g. maternal age at conception, pre-existing conditions like hypertension, diabetes. Multiple pregnancies can also attribute to these risks in IVF pregnancies[5].

## METHODS AND MATERIALS:

A retrospective case study was conducted in Wexham park Hospital. Total of 62 patients with IVF conception who were seen in our antenatal clinic referred by community midwives as high risk pregnancy were recruited in this study in year 2017. Data was collected from maternity hand-held notes. Electronic record of patient care was also used to retrieve data for completion of information. 12 patients

notes were either missing or incomplete, so were not included in the study. Data was obtained from 40 women and entered electronically on a pre-designed spreadsheet and information was analysed by Trust audit department.

First trimester was counted up to 12 +0 weeks, second trimester started from 13+0 weeks, and third trimester from 26+0 weeks of pregnancy until 40+0 weeks. Preterm delivery was defined as delivery before 37+0weeks.

Risk assessment of each pregnancy was completed by community midwife at booking appointment. Women who conceived through IVF treatment and referred to hospital antenatal clinic after a dating scan by community midwives as deemed high risk, were included in this study.

There was limitation of this study as to whether donor or native oocyte or sperm was used for conception was not specified. Similarly, there was no mention of fresh or frozen cycle, single or double embryo transfer.

#### OBJECTIVES:

The main objective of the study was to review patient journey through antenatal period and labour, and obstetric outcome of IVF pregnancy in our unit. This would enhance our understanding of how the maternity services for women who achieve conceptions through IVF treatment could be optimised.

#### RESULTS:

Regarding patient characteristics,(Table 1) about 80% of pregnant women were either from white British or Asian origin and the rest were from other ethnicity groups. This information was obtained from booking information by community midwives. Around 72% of patients were between 30 to 40 years of age and 18% were from the age bracket of 40-50 years which explains relatively small incidence of infertility among older women in our cohort.

BMI was calculated at booking by community midwives and those at high risk were prescribed venous thromboembolism prophylaxis . 70% of women had BMI range between 20-30 and 20% had BMI more than 30. Only 5% of women had BMI less than 20 and BMI was not recorded in remaining 5%.

**Table 1 : patient characteristics**

Ethnicity	Asian / British	80%
	Others	20%
Body mass index (BMI)	<20	5%
	20-30	70%
	>30	20%
	Not recorded	5%
Age	30-40(years)	72%
	>40 years	18%
	<30 years	10%

Primary infertility (Table 2) was seen in 43% of pregnant women whereas 57% had secondary infertility. Among the secondary infertility group, 57% had one or more children from previous pregnancies.

Among parous women, previous pregnancy details were taken. 78% had conceived spontaneously (natural conception) and 9% of women required IVF treatment to achieve conception previously.

**Table 2:**

<b>Primary infertility</b>	43%
<b>Secondary infertility</b>	57%
Previous no child	43%
Previous one child	52%
Previous two child	5%
<b>Previous conception</b>	
Spontaneous	78%
IVF conception	9%

Complications during each trimester in antenatal period as shown in Table 3, was recorded as abdominal pain, per vaginal bleeding, hypertension , diabetes , and preterm labour and preterm delivery after 24 weeks. In first trimester, 5% of pregnancies ended in spontaneous miscarriage compared to 3% in second trimester. Half of these pregnancies were dichorionic twin pregnancies.

Patients presentation in hospital with per vaginal bleeding or abdominal pain as main complaints in early pregnancy was seen in only 3% in first trimester and 10% in second trimester of pregnancy.

**Table 3: complication in 1<sup>st</sup> & 2<sup>nd</sup> trimester**

	1 <sup>st</sup> trimester	2 <sup>nd</sup> trimester
Pain abdomen	3%	10%
Per vaginal bleeding	3%	10%
Miscarriage rate	5%	3%

Booking blood pressure was normal in most women, only one woman had chronic hypertension which was controlled with labetalol. Aspirin was started in 8% of cases in first trimester based on risk assessment at booking by community midwives while 70% of pregnant women were advised to start aspirin after 12 weeks in hospital antenatal clinic by obstetrician.

Cyclogest pessary was prescribed in 5% of women till 12 weeks of pregnancy. 5% of women was advised to take Dalteparin based on their thromboembolic risks as recommended by the Royal College of Obstetricians and Gynaecologists guideline on reducing the risk of venous thromboembolism during pregnancy and the puerperium <sup>18</sup>.

Combined screening test results were low in 92.5%, only 1 patient had low PAPP-A detected in first trimester screening test. However, in 2.5% of females

screening test result could not be obtained from patient notes.

Fetal abnormality was detected in 3 women at their anomaly scans. 1 fetus had complete agenesis of corpus callosum and ventriculomegaly, 1 had transposition of great arteries. 1 fetus of a DCDA Twin pregnancy was diagnosed with Fallots Tetralogy and severe IUGR.

In 3 (8%) women, placenta remained low as praevia and required delivery by elective Caesarean section at 38 weeks.

Glucose tolerant test was positive in 30% of cases (Table 4), among them 20% developed gestational diabetes controlled with diet only, while 5% of cases required metformin and 5% had insulin in addition to metformin.

**Table 4: Complications**

Combined screening test	Low risk	92.5%
	High risk	2.5%
	Patient refused	2.5%
	Data not obtained	2.5%
Fetal abnormality	Not detected	92%
	Detected	8%
Glucose tolerance test	Normal	70%
	GTT Positive controlled on Diet	20%
	GDM controlled on Metformin	5%
	GDM on Insulin & metformin	5%

One woman delivered a IUGR baby diagnosed on serial growth scans by an elective Caesarean section at 32 weeks. The woman conceived as DCDA pregnancy, had one fetal demise at seven weeks and her pregnancy continued as a singleton pregnancy.

Around 65% of women delivered at term (37-40 weeks) and 12% delivered post dates (40-42 weeks). Regarding early delivery, 23% of women had preterm labour before 37 weeks. Among them 5% delivered before 32 weeks of gestation as shown in Table 5.

**Table 5: Gestation at delivery**

32+1-36+0 weeks	16%
=/<32+0 weeks	5%
36+1-37 +0 weeks	2%
37+1- 40+0 weeks	65%
=/>40+1 weeks	12%

Table 6 explains the mode of delivery. 57% of women were delivered by Caesarean section. Emergency lower segment Caesarean section rate was slightly higher than elective Caesarean section i.e. 30% vs.27%. Spontaneous vaginal delivery was

seen in 38% of cases while in 5% vaginal delivery was assisted with forceps.

**Table 6: Mode of delivery**

Spontaneous vaginal delivery	38%
Instrumental delivery	5%
Emergency lower segment caesarean section	30%
Elective lower segment caesarean section	27%

## DISCUSSION:

Artificial reproductive technology (ART) including IVF has been a miracle for sub fertile couples in the last few decades. These pregnancies are recognized as high risk in terms of maternal and perinatal outcome, and warrant monitoring under specialist care [6,7]. Our study is focused on outcome of IVF pregnancies in a consultant led maternity care in a NHS Hospital and pregnancies are monitored with Trust maternity care policies. Although the majority of IVF pregnancies have satisfactory obstetric outcome, there are a number of background high risk factors in this group of patients that may reflect lower threshold for obstetric intervention [8].

Advancing age is naturally associated with increased incidence of chronic diseases such as chronic hypertension, cardiac diseases and diabetes and thus older women who undergo assisted reproduction treatment are more likely to start their pregnancy with a chronic medical condition [9]. In our cohort, almost 70% of women had healthy BMI between 20 and 30. Only 1 (2.5%) patient was identified as chronic hypertension at booking and her BP was stable on labetalol, she subsequently developed pre-eclampsia in third trimester. Significantly high (30%) number of women developed GDM at some stage in pregnancy, 1 women had positive GTT at 12 weeks who also had developed GDM in a previous pregnancy, 2 women were diagnosed at 28 weeks screening test. 9 women had positive GTT in between 28 and 36 weeks on repeat tests because of persistent glycosuria +/- fetal macrosomia diagnosed on serial fetal growth scans. In England and Wales, up to 5% of women in general population have either preexisting diabetes or gestational diabetes [10]. The increased maternal and perinatal risks in IVF population must be considered prior to attempts for assisted conception, and the transfer of more than one embryo should be avoided in women with a pre-existing maternal medical condition [6].

Congenital abnormalities are seen in higher numbers in IVF pregnancies. A recent study by Qin et al [11], has shown the highest number of congenital abnormalities and admission to neonatal intensive care. One cohort study reported a significantly increased rate of structural abnormalities (anorectal malformations, congenital cardiac lesions, nervous



system and genital structural abnormalities) [12]. In our study, the incidence of structural anomalies was around 8% which included complete agenesis of corpus callosum, ventriculomegaly, absent ductus venosus, transposition of great arteries and Fallots Tetralogy.

Birth weight and mean gestational age at delivery between children born after single embryo transfer in IVF and children conceived without medical assistance are almost the same [13]. In our study, 85% of pregnancies were monitored with fetal growth scans at 32 and 36 weeks of pregnancy, only 1 woman developed significant IUGR requiring delivery around 32 weeks of pregnancy with steroid cover who had continued as a singleton pregnancy following a DCDA twin conception.

Multiple gestation is the single most important determinant of pregnancy outcome, either from natural or assisted conception. The adverse pregnancy outcome specific to multiple pregnancy includes pregnancy induced hypertension, gestational diabetes, uterine bleeding, placental complications e.g. placental abruption, placenta praevia, vasa praevia, prenatal hospitalization and primary caesarean section [14]. In 2011, nearly one in five (19.8%) of IVF deliveries in UK involved a multiple birth [15]. In our study, 5% of pregnancies ended in miscarriage in first trimester and among half of them were conceived as twin pregnancies.

Placenta praevia and placenta accreta are associated with high maternal and neonatal morbidity and mortality. The estimated incidence is 0.5%, the rates have increased due to maternal age and use of assisted reproductive technology [16]. In our study, the incidence of placenta praevia at term in singleton pregnancies was significantly high (8%).

The incidence of preterm labour in England and Wales in 2012 was around 7.3% [17]. Preterm labour is associated with high risks of early and late neonatal morbidity and increased risk of neuro-disability. Prematurity is the other risk factor in IVF pregnancies reported in literature as 23%, consistent with findings in our cohort of women.

### CONCLUSION:

With better understanding of the science around assisted conception, advancement of technology and need-based service provision to subfertile couples, number of successful pregnancies and healthy babies born through IVF are increasing day by day. This could be attributed to many factors including patient characteristics, fetal growth potential and optimum environment. Through regulation of IVF treatment modalities and provision of tailored maternity care to IVF conceptions, satisfactory maternal and perinatal outcome can be achieved.

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