



OBSTETRIC AND PERINATAL OUTCOMES FOLLOWING INVITRO FERTILIZATION (IVF) PREGNANCY AT THE UNIVERSITY OF PORT HARCOURT TEACHING HOSPITAL: A 5 YEAR REVIEW.

Kinikanwo Innocent Green¹, Preye Owen Fiebai¹

¹ Department of Obstetrics and Gynaecology, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

Correspondence:

Email: kinikanwo.green@uniport.edu.ng

ABSTRACT

Background: *In vitro* fertilization technique is one of the many assisted conception treatment options that has helped to reduce the burden of infertility in over two decades. Pregnancies resulting from IVF are noticed to have more burdens of morbidities than pregnancies that are naturally conceived.

Objectives: To evaluate the fetomaternal outcome of pregnancies conceived from invitro fertilization and were managed and delivered at the University of Port Harcourt Teaching Hospital (UPTH).

Materials and Methods: This was a 5-year retrospective study of all pregnant women who had conceived via in vitro fertilization, assisted conception and had obstetric care at the University of Port Harcourt Teaching Hospital (UPTH). The Statistical package Microsoft excel 2019 was used for analysis of data from patients case records.

Results: The incidence of deliveries from IVF pregnancy was 0.67%. There were 24(52.17%) multiple pregnancies resulting from IVF deliveries and 14 (30.43%) were twin deliveries. Among the patients 7(13.04%) had severe pre-eclampsia and 3(6.25%) each had gestational diabetes mellitus and primary post-partum haemorrhage respectively. There was a 100% caesarean section rate and 34.78% of the women had their neonates admitted in the special care baby units.

Conclusion: *In vitro* fertilization pregnancies are associated with increased risk for caesarean section, adverse maternal and neonatal outcomes due to increase in fetomaternal morbidities.

Keywords: *In vitro* fertilization pregnancy, maternal outcome, fetal outcome, Port Harcourt.

INTRODUCTION

Infertility is a disease of the reproductive system defined as the failure to achieve clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.¹ Global estimates suggest that nearly about 72.4 million couples experience fertility problems.² It affects 8-15% of the world's population, varying from region to region.^{2,3} The rate of infertility varies in sub-Saharan Africa, affecting 10-30% couples in Nigeria.⁴

In vitro fertilization (IVF) has been popularized as one of the commonest safe and effective methods of treatment of infertility for over two decades.^{5,6} Since after the birth of the first baby via IVF over 40 years ago, over 8 million children have been born globally by IVF.⁷

Pregnancies achieved following treatment with IVF have been associated with increased risk of adverse maternal and perinatal outcomes.^{8,9} It is clear that infertile women treated with IVF have higher risk of conceiving multiple gestation which increases risk of adverse pregnancy outcomes.^{10,11} This calls for an advocacy for a national policy for IVF regulation and adoption of a single embryo transfer method which will in turn clampdown on the maternal and perinatal morbidity and mortality associated with multiple gestation.

However, singleton gestations achieved by IVF have shown an increased risk of adverse pregnancy outcomes when compared to the general population.¹² Studies have demonstrated increased risk of early pregnancy bleeding, antepartum hemorrhage,

low/very low birth weight, neonatal morbidity, congenital heart defect, still birth and neonatal mortality among women who had singleton pregnancy conceived by IVF.^{12,13} Orazulike et al reported similar outcomes to other studies in a tertiary institution in South-South, Nigeria.¹⁴ More so, a systematic review and meta-analysis of singleton pregnancies resulting from in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) has shown an increased risk in hypertensive disorders in pregnancy, antepartum hemorrhage, gestational diabetes mellitus, increased caesarean section rate, increased rate of induction of labour, preterm rupture of membranes, congenital abnormalities and perinatal mortality.¹⁵

The actual determinant(s) of the disparity in outcomes between spontaneously conceived pregnancies and those by IVF is/are not clear. However, Olivennes et al has demonstrated that the adverse pregnancy outcome associated with IVF is not due the IVF itself but due to ovarian stimulation.¹⁶

This study reviewed the various IVF pregnancy deliveries at the UPTH and the fetomaternal outcomes.

MATERIALS AND METHODS

This was a 5-year retrospective study of all pregnant women who had conceived via in vitro fertilization with embryo transfer and had obstetric care at the University of Port Harcourt Teaching Hospital (UPTH) between January 1, 2017 and December 31, 2021.

This study was carried out at the obstetric unit of the UPTH, which is a tertiary hospital with an average of 1500 deliveries conducted

annually. It has one of the highest delivery rates among all the health facilities in Rivers State. The hospital has 890 bed spaces with the obstetric unit having a total of 135 beds.

The women were referred from the assisted conception unit of UPTH and private clinics that practice assisted conception in and around Port Harcourt environs. In Southern Nigeria, the assisted reproductive technology has been existent since 2004 and has been mostly driven by the private hospitals. Only women who delivered after the gestational age of foetal viability taken as 28 weeks in our environment and seen up to six weeks of the puerperium were included in the study.

The theatre records, delivery registers and case notes of these women over the period under review served as the source of data from where the variables analysed were retrieved. These outcome variables included maternal parameters: i.e. socio demographic features, pregnancy complications, mode of delivery and outcome. Foetal parameters included gestational age at birth, number of babies, birth weight, APGAR scores and indication for special care baby unit (SCBU). The data collated was entered into a spread sheet and analysed with Microsoft excel 2019.

RESULTS

Forty six pregnancies carried beyond the age of viability (twenty eight weeks) following in vitro fertilization (IVF) were managed and delivered during the period under review. There were a total of 6868 deliveries between 2017 and 2021, giving an incidence of delivery

following IVF pregnancy of 0.67%.The mean maternal age was 38 ± 5.44 (SD) years and 44(95.65%) of the mothers had tertiary level of education. Table 1 shows the socio-demographic characteristics of the women.

Table 2 shows the types of pregnancies resulting from IVF, there were 22 (47.83%) singleton deliveries and 14 (30.43%) twin deliveries. It also shows a 100% caesarean delivery rates. It also shows the indication for caesarean sections.

Table 3 shows obstetric complications during the pregnancy and after delivery. There were no complications in 27 (58.7%), while 7(13.04%) had severe pre-eclampsia and 3(6.25%) each had gestational diabetes mellitus and primary post-partum haemorrhage respectively. One patient (2.17%) had chronic hypertension with covid-19 in pregnancy.

The mean gestational age at delivery was 38.23 ± 5.44 (SD). The mean birth weights for singleton, twin, triplet and quadruplet deliveries were 3.34 ± 0.47 (SD), 2.28 ± 0.81 (SD), 2.11 ± 0.41 (SD) and 1.58 ± 0.20 (SD) respectively. Table 4 shows delivery outcome of 69 babies, 68 live babies and one intrauterine fetal death of one of a twin. They were 14(63.64%) of male singleton and 18 (75%) of male twin deliveries, whereas there were 12(80%) of female triplet and 6(75%) of female quadruplet deliveries. Table 4 also shows the different APGAR scores at first and fifth minute.

Table 1

Socio-demographic characteristics

Variable	Frequency	Percent(%)
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N=46

Age		
25-29	1	2.17
30-34	13	28.26
35-39	15	32.61
40-44	12	26.09
45-49	3	6.52
50-55	2	4.35
Marital status		
Married	46	100.00
Level of education		
Secondary	2	4.35
Tertiary	44	95.65
Occupation		
Banker	1	2.17
Business	16	34.78
Civil servant	9	19.57
Housewife	17	36.96
Teacher	3	6.52
Tribe		
Igbo	25	54.35
Ijaw	3	6.52
Ikwerre	7	15.22
Isoko	2	4.35
Ogoni	2	4.35
Urhobo	2	4.35
Yoruba	5	10.87
Religion		
Christian	46	100.00
Parity		
0	24	0.00
1	13	59.09
2	6	27.27
3	3	13.64
Previous pregnancy losses		
0-1	33	71.74
2-3	10	21.74
4-5	2	4.35
6-7	1	2.17
Total	46	100%

Table 2.1: Pregnancy History

Variable	Frequency N=46	Percent (%)
Type of pregnancy		
Singleton	22	47.83%
Twin	14	30.43%
Triplets	7	15.22%
Quadruplets	3	6.52%
Gestational age at delivery		
30-32	3	6.52%
33-35	12	26.09%
36-38	27	58.70%
39-41	4	8.70%
Mode of delivery		
Elective caesarean section	24	52.17%
Emergency caesarean section	22	47.83%

Table 2.2: Indications for caesarean section delivery and estimated blood loss

Variable	Frequency	Percent (%)
Indication for CS Delivery		
Abruptio placenta with live babies	1	2.17%
Antepartum Haemorrhage due to placenta	1	2.17%
Placenta Previa in Quadruplets pregnancy		
Cephalo pelvic disproportion in labour	1	2.17%
Fetal distress	1	2.17%
IVF pregnancy with co-existing uterine fibroids in pregnancy	2	4.35%
IVF pregnancy, 1 previous CS	4	8.70%
IVF pregnancy, Twin gestation, non cephalic leading twin	2	4.35%
IVF, severe PIH	1	2.17%
IVF, subfertility, advanced maternal age	1	2.17%

IVF,IUFD of second twin	1	2.17%
maternal request	7	15.22%
Previous myomectomy	7	15.22%
Prolonged preterm prelabour rupture of membranes in an elderly primigravida with IVF twin pregnancy	2	4.35%
Quadruplets in labour	1	2.17%
Quadruplets pregnancy in labour	1	2.17%
Severe pre-eclampsia with unfavourable cervix	7	15.22%
Transverse lie	1	2.17%
triplet gestation	1	2.17%
triplet gestation	1	2.17%
Triplets gestation in labour	2	4.35%
Twin gestation and 1 previous CS	1	2.17%
Estimated Blood Loss (ml)		
250-349	2	4.35%
350-449	11	23.91%
450-549	13	28.26%
550-649	7	15.22%
650-749	2	4.35%
750-849	7	15.22%
950-1049	2	4.35%
1150-1249	1	2.17%
1450-1549	1	2.17%
Grand Total	46	100.00%

Table 3: Obstetric Complication

Variable	Frequency	Percent(%)
Obstetric complication		
Chronic hypertensnion and Covid-19 in pregnancy	1	2.17%
Demise of second twin at 27 weeks GA	1	2.17%
Gestational Diabetes Mellitus	3	6.52%
None	27	58.70%
Pregnancy induced hypertension	1	2.17%
Preterm prelabour rupture of	2	4.35%

membranes		
Primary post partum	3	6.52%
Haemorrhage		
Severe pre-eclampsia	7	15.22%
Transverse lie at term	1	2.17%
Past Medical History		
Chronic hypertension	2	4.35%
None	44	95.65%
Past Surgical History		
2 previous myomectomy	1	2.17%
Cervical polypectomy	1	2.17%
None	36	78.26%
Previous Caesarean section	5	10.87%
previous myomectomy	3	6.52%
Total	46	100%

Table 4: Fetal Outcome

Table 4.1

Variable	Frequency	Percent (%)
Sex (singleton)		
Female	8	36.36%
Male	14	63.64%
Total	22	100
Sex (twin)		
Female	6	25.00%
Male	18	75.00%
Total	24	100
Sex (Triplets)		
Female	12	80.00%
Male	3	20.00%
Total	15	100.00%
Sex (Quadruplets)		
Female	6	75.00%
Male	2	25.00%
Total	8	100.00%
Birth weight(singleton)		
1.9-2.4	1	4.55%

2.4-2.9	1	4.55%
2.9-3.4	8	36.36%
3.4-3.9	10	45.45%
3.9-4.4	2	9.09%
Total	22	100.00%
Birth weight (Twin)		
0.5-1	1	3.57%
1-1.5	4	14.29%
1.5-2	3	10.71%
2-2.5	6	21.43%
2.5-3	8	28.57%
3-3.5	4	14.29%
3.5-4	2	7.14%
Total	28	100.00%
Birth weight (Triplet)		
1.3-1.8	3	14.29%
1.8-2.3	12	57.14%
2.3-2.8	5	23.81%
2.8-3.3	1	4.76%
Total	21	100.00%
Birth weight (Quadruplets)		
1.1-1.6	7	58.33%
1.6-2.1	5	41.67%
Total	12	100.00%

Table 4.2.1

Variable	Frequency	Percent (%)
APGAR scores at first minute (singleton)		
3-4	1	4.55%
5-6	1	4.55%
7-9	20	90.91%
Total	22	100.00%
APGAR scores at first minute (Twin)		
0-1	1	3.57%
2-3	2	7.14%
6-7	12	42.86%

8-9	13	46.43%
Total	28	100.00%
APGAR scores at first minute (Triplet)		
4-5	1	4.76%
6-7	7	33.33%
8-9	13	61.90%
Total	21	100.00%
APGAR scores at first minute (Quadruplets)		
3-4	2	16.67%
5-6	2	16.67%
7-8	8	66.67%
Total	12	100.00%

Table 4.2.2

Variable	Frequency	Percent (%)
APGAR scores at fifth minute (singleton)		
7-9	22	100.00%
Total	22	100.00%
APGAR scores at fifth minute (Twin)		
0-1	1	3.57%
4-5	2	7.14%
6-7	1	3.57%
8-9	24	85.71%
Total	28	100.00%
APGAR scores at five minutes Triplets		
7-9	21	100.00%
Total	21	100.00%
APGAR scores at fifth minute Quadruplets		
6-7	2	16.67%
8-9	10	83.33%
Total	12	100.00%

Table 4.3

SCBU Admission		
No	30	65.22%
Yes	9	19.57%
Yes	1	2.17%
Yes both babies (Twin)	4	8.70%
Yes, for all quadruplets	2	4.35%
Indication for SCBU admission		
Infant of a diabetic mother	1	2.22%
Infant of Rh negative mother, prematurity	1	2.22%
Nil	29	64.44%
Prematurity and low birth weight	11	24.44%
Risk for sepsis	1	2.22%
Severe birth asphyxia	2	4.44%

DISCUSSION

The use of assisted reproductive techniques (ART), including in vitro fertilization techniques (IVF) for treatment of infertility continues to gain prominence in clinical practice as an essential, acceptable and important means of helping patients struggling to achieve child birth. This assistance in conception has been noticed by many researchers to be associated with adverse maternal and perinatal outcomes.^{8,14,17-21} Although the underlying mechanisms involved in the association between IVF and poor perinatal outcomes remains uncertain, there is a great body of evidence in the literature hypothesizing that most of these differences stem from the consequences associated with controlled ovarian stimulation on endometrial receptivity.¹³

In this study we highlight an increase in the incidence rate of assisted reproductive technique (ART) pregnancy deliveries of 0.67% from the 0.3% seen in the study by Orazulike et al in the same facility.¹⁴

The mean age of the women in this study was 38 ± 5.44 and was similar to the study by Orazulike et al where the mean age was 38 ± 7.3 .¹⁴ It was also not far from the mean age of participants in a study by Hussein Sabban et al where most of the participants were aged above 35 years.¹⁸ This highlights the fact that women start to present to the hospital for fertility care at a later age in their reproductive career after trying different unorthodox methods of seeking conception or out rightly beginning a reproductive career at an advanced age.^{19,22,23}

ART was associated with increased frequency of multiple pregnancies, preterm deliveries

and 41.3% of the patients had obstetric complications like Severe pre-eclampsia, gestational diabetes, preterm prelabour rupture of membranes and also primary post-partum haemorrhage among others. This is similar pattern noticed in various studies.^{8,9,14,17,18,21,24,25} These complications are due to advanced maternal age, multiple pregnancies and increased risk of caesarean delivery.

In this study all the patients had caesarean section delivery. There is a known association between ART and caesarean section noted in a study by Charlotte et al.²⁴ Also a meta-analysis by Jackson show an increased risk of planned caesarean section following ART.¹⁵

This increase in the frequency of C/S delivery is more often due to complications like pre-eclampsia or multiple pregnancies, advanced maternal age, and even maternal request. One can also allude that there may be an increased stress of the obstetrician and the patient because of what is often termed “precious pregnancy”, due to longer duration of infertility and amount of money spend for ART.

Among the women who delivered, 34.78% had their babies admitted into the special baby unit after delivery. There was a risk of low birth weight which can be linked to multiples pregnancies and preterm deliveries. The common reasons for special care baby unit (SCBU) admission include birth asphyxia, prematurity and low birth weight. Similar fetal outcomes has been notice in other similar studies.^{8,15,17–19,21}

CONCLUSION

Pregnancies conceived from in vitro fertilization and embryo transfer were mostly among women of advanced maternal age and

there have been an increased number of IVF pregnancy deliveries in UPTH. The pregnancies were associated with multiple orders, preterm deliveries, low birth weight and admission of neonates into special care baby units.

The high level of caesarean delivery was noted to be due to maternal factors, complications and social obstetric consideration for ‘precious’ pregnancy.

STUDY LIMITATIONS

Limited information from case files retrieved as some of the IVF conceptions occurred outside the facility. Some the babies were nursed outside the facility, making follow up information difficult to sort.

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