Case Report

Quadruplet pregnancy following transfer of 3 embryos: A case report

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ABSTRACT

Multiple pregnancy is a known complication of *in-vitro* fertilization and embryo transfer (IVF-ET). It is usually associated with serious perinatal morbidity and/or mortality as well as significant maternal morbidity and efforts to reduce these has led to the concept of elective single embryo transfer (ESET) in developed countries, this concept has not been entrenched in the practice in Nigeria. We report a case of quadruplet pregnancy following the transfer of three embryos following IVF and reviewed the relevant literature.

Key words: Complications; *in-vitro* fertilization; pregnancy; quadruplets.

Introduction

Higher order multiple pregnancies (HOMP) are a serious complication of *in-vitro* fertilisation (IVF). In developed countries, efforts are being made to reduce the number of embryo transferred following the treatment, but in Nigeria there are no clear guidelines on the number of embryo that can be transferred resulting in a high incidence of HOMP in IVF treatments in Nigeria. We report a case of quadruplet pregnancy following the transfer of 3 embryos.

Case Report

Mrs. A.I was a 48-year-old married woman who was cohabiting with her husband for the past 17 years without conception despite unprotected sexual intercourse about three times per week which was said to be satisfactory. Husband had no children outside the marriage and had no previous pregnancy.

She attained menarche at 18 years, menstruated for 5 days in a regular 28-day menstrual cycle until March 2013. She had no menorrhagia, dysmenorrhea, dyspareunia, or postcoital bleeding. There was no intermenstrual bleeding, or postmenopausal bleeding. She was aware of modern use of contraceptives and used none. There was no previous pap smear. There were no previous abortions or treatments for sexually transmitted infections or pelvic inflammatory disease.

She had no anterior neck swelling, heat or cold intolerance, and palpitations or fine tremors. There were no recurrent frontal headaches, changes in sense of smell, or abnormal milky nipple discharges. There was no increasing acne, deepening of voice, or abnormal male hair pattern.

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She had two previous myomectomies in 1999 and 2010; had at least one unit of whole blood transfused on both occasions. She was not a known hypertensive, diabetic, peptic ulcer disease, or asthmatic patient. She previously used clomiphene citrate and vitamin E routinely and there were no known drug allergies.

She was married to a 52-year-old trader in a monogamous family setting. She did not consume alcohol nor smoked cigarettes.

Her husband was able to initiate and sustain an erection and also ejaculate. He did not wear tight underwear and there was no previous abdominal or groin surgery. He was not a known hypertensive or diabetic patient. He consumed alcohol occasionally, but smoked for a period of 5 years about 20 years ago.

Examination revealed a middle-aged woman, conscious and alert, not pale, anicteric, acyanosed, not dehydrated with no pedal edema.

Anthropometric measurements: Height = 1.58 m; Weight = 65 kg, and BMI = 26.0 km/m^2 (overweight)

Examination of the head, neck, and respiratory system did not reveal any abnormalities.

Her pulse rate was 110 bpm, regular with thickened arterial wall, and locomotor brachialis. Blood pressure was 180/110 mmHg; Apex beat was in fifth left intercostal space lateral to mid-clavicular line. Heart sounds S4, S1, and S2 only, no murmur.

The abdomen was full, soft moved with respiration. There were two previous midline infraumbilical to suprapubic scar. There was no area of tenderness, no ascites demonstrable, and bowel sounds were normoactive.

Vaginal examination revealed a normal female external genitalia, cervix was healthy looking deficient in the posterior lip with a mild stenosis of the internal os which overcomes with resistance. Uterus was anteverted or slightly deviated to the right and depth of 7 cm.

Based on the history and examination findings, an assessment of primary infertility in a postmenopausal woman with hypertension was made.

She was counselled and scheduled for *in vitro* fertilization, egg donation, and embryo transfer. She was immediately commenced on antihypertensives and when the blood pressure normalized she was commenced on hormone replacement therapy.

The couple had some investigations done and the results are shown on Tables 1 and 2.

She had hormonal profile which revealed follicle stimulating hormone (FSH) = 103.20 mIU/ml (elevated); luteinizing hormone (LH) = 65.42 mIU/ml (elevated); prolactin = 341.80 uIU/ml, and estradiol = 5.0pg/ml; a postmenopausal state.

She subsequently had *in-vitro* fertilization and Day 5 blastocyst transfer on 7 August 2014. Three expanded blastocysts were transferred into the endometrial cavity with the aid of a Labotect catheter under ultrasound guidance. Embryo transfer was smooth.

She had luteal phase support with IM progesterone in oil 100 mg OD, PV cyclogest pessaries 400 mg BD, PO progynova 6 mg OD, and PO folic acid 5 mg OD.

14th day post transfer, serum βHCG was positive, and hormonal support was continued until 12 weeks gestation.

Pelvic ultrasound done at estimated gestation age of 10 weeks showed three gestational sacs with four identifiable fetal poles and crown-rump lengths approximately 10W + 2D. She was then schedule for a prophylactic cervical cerclage after 12 weeks gestation which she had.

She booked pregnancy at gestational age of 14W + 5D, she received two doses of tetanus toxoid and intermittent

Table 1: Results of some investigations carried out by couple

Tests	Husband	Patient
Chlamydia	Non-reactive	Non-reactive
RVS	Non-reactive	Non-reactive
HBsAg	Negative	Negative
HCV	Negative	Negative
VDRL	Negative	Negative
Blood Group	O Negative	B Positive
Genotype	AA	AA
RBS	6.2 mmol/L	6.4 mmol/L

Table 2: Result of husband's semen analysis

Appearance	Creamy-white
Viscosity	Moderate
Volume	3.5 ml
Motility	Active – 63%; Sluggish – 12%; Non-motile – 25%
Morphology	Normal – 40%; Abnormal – 60%
RBC	1-2/hpf

preventive therapy for malaria at 22W + 5D and 26W + 5D respectively. She was admitted for bed rest in the hospital at 26 weeks gestation and was commenced on prophylactic steroid IM dexamethasone 12 mg BD weekly.

On 21 February 2015, at gestational age of 30W + 2D she started having preterm labor and was scheduled for an emergency cesarean section and delivered a set of female quadruplets; T1 weighed 1.2 kg APGAR $9^1 10^5$; T2 weighed 1.25 kg APGAR 9^1 10^5; T3 weighed 1.4 kg APGAR 10^1 10^5; T4 weighed 1.2 kg APGAR 9^1 10^5. Babies were immediately admitted in the neonatal intensive care unit, placenta was delivered by controlled cord traction, and estimated blood loss was 800 ml. Babies were admitted on account of prematurity and low birthweight. Mother was discharged on sixth postoperative day, postoperative condition was uneventful with PCV = 34%. Babies were admitted for a period of 4 weeks after which they were discharged home in good condition. Weight at discharge was 1.7 kg, 1.8 kg, 2.4 kg, and 1.7 kg, respectively. The picture of the babies after discharge are shown in Figure 1.

Six weeks post-delivery both mother and babies were seen and in satisfactory conditions. Babies were commenced on immunization according to the National Programme for Immunization.

Discussion

The high frequency of multiple births is the main factor which leads to adverse outcome in IVF/intracytoplasmic sperm injection (ICSI) treatments. Transfer of two embryos does not diminish the chance of a birth when compare with three embryo transfer, if more than four embryos are available for transfer.[1] However, in many countries more than two embryos are still generally transferred especially in IVF centers in Nigeria.

This woman had three embryo transferred because of her age coupled with two previous myomectomies which we thought will diminish the endometrial receptivity as a result of scarring, but she ended up with a quadruplet pregnancy, hence there is the need to have a limit to the number of embryo transferred in IVF practice in Nigeria.

In the USA, the average number of embryos transferred is four and the multiple pregnancy rate (PR) is ~40% in IVF/ICSI treatments.[2]

It has been estimated that one embryo is more cost effective than two embryo transfer when all the cost associated with multiple gestations are taken into account.[3]

Multiple pregnancies cause several well-documented pathologies, extensively reviewed everywhere.[4] They comprise a maternal risk for obstetric complications, hypertension, preeclampsia, preterm labor, anemia, and an increased cesarean section rate; fetal or neonatal risk for increased mortality, lower gestational age, lower birth weight, respiratory distress syndrome, necrotizing enterocolitis, sepsis, intracranial hemorrhage, congenital malformations, the twin-twin transfusion syndrome, cerebral palsy, and long-term neurological complications; and family complications of psychological, social, and financial nature.[5]

Following birth, multiples suffer from increased rates of learning difficulties and perceptual disabilities.[6] Growth-restricted twins are at increased risk of poor postnatal growth and speech and behavioral problems compared with their appropriately grown siblings.[7] Further, the differences in locomotive, hearing, speech, and practical reasoning scores increase with the degree of birth weight discordance.[8] Similarly, increased morbidity and mortality has been reported in IVF twins compared with IVF singletons.[9] Compared with IVF singletons, IVF twins have a 10-fold increased risk of preterm (<37 weeks) delivery, a 7-fold increased risk of delivery before 32 weeks' gestation, and a 12-fold and 5-fold increased risk of birth weight <2500 g and <1500 g, respectively. The risk of stillbirth is doubled.[9] However, incidence of neurological sequelae appears to be similar.[10]

Mrs. A.I has a set of quadruplets following IVF with transfer of three embryos and luckily the babies did not suffer any of the

Figure 1: The Quadruplets after discharge from NICU

aforementioned complications. Many IVF patients in Nigeria are not that lucky and many of the higher order multiple pregnancies (HOMP) end up in miscarriages or extreme premature births with neonatal complications.

Transferring just one embryo even of ideal morphology in an ideal recipient was a taboo, because it was feared that the PR would drop below that of our nearest neighbor or below the layman's and the media's expectations.[5] Even if the society is willing to pay for the extra costs incurred, money can never restore health irreparably lost and even if it could, society should ask whether this is really needed, provided chances to conceive after IVF/ICSI are not substantially decreased without running those risks. There is a strong philosophical argumentation putting the responsibility for our children's good health at the start of their life on all those involved in IVF/ICSI (patients, health care providers, health insurers, and politicians).[5]

There is an urgent need for practitioners in the fertility health care units in Nigeria to come up with guidelines on the number of embryo to transfer so as to reduce the incidence of HOMP in Nigeria.

In developed countries, the practice of elective single-embryo transfer has been advocated and studies have shown that this does not reduce PR especially in younger women.[11]

Conclusion

In conclusion there is a need to reduce the number of higher order multiple birth in IVF practice in Nigeria and the way to achieve this is through the production of evidence based practice guidelines by the stakeholder in the professional association.

Adoption of the ESET will drastically reduce the incidence of multiple pregnancy, but may not eliminate it completely due to monozygotic twining, this will result in an improved quality of life for babies born through this technology and hence the parental satisfaction.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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