Spontaneous Foetal Reduction In Multiple Pregnancies Complicating Fertility Treatment: Descriptive Study Of Pregnancy And Fetal Outcomes In A Low Resourse Setting

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Citation

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Abstract

Objective: Spontaneous reduction resulting from missed abortion of one or more of the foetuses before the 12th week of pregnancy could affect obstetrics outcome. This study sought to analyse pregnancy and foetal outcome following vanishing foetal event in multifoetal pregnancies conceived through assisted and non-assisted technology fertility treatment.Methods: A 5 year prospective observational study conducted In Ahmadu Bello University Teaching Hospital Zaria, 345 Aero medical Hospital Kaduna and Alba Clinics and Medical Centre Kaduna. Patients either conceived with clomiphene citrate enhanced fertility treatment or through assisted reproductive technology (ART) treatment. Results: Fifteen cases were managed, of which 9 (60%) were non-ART conceptions and 6 (40%) ART conceptions. The 9 non – ART pregnancies were all twins spontaneously reduced to singletons, while the 6 ART pregnancies comprised of 4 (66.7%) twins reduced to singleton. 1 (16.7%) triplet reduced to twin and 1 quintuplet (16.7%) reduced to quadruplet. Outcome of 13 pregnancies reduced to singleton was favourable with 1 (7.7%) infant death due to complications of congenital heart disease. Triplet pregnancy reduced to twin was complicated with severe hypertension in pregnancy and spontaneous abortion at 19 weeks while the patient with quintuplet pregnancy reduced to quadruplet delivered at 7 months preceded by preterm premature rupture of membrane; 3 neonatal deaths was recorded. Conclusion: Outcome of vanishing foetus syndrome in higher order multiple pregnancy was associated with poor foetal outcome, however this may be unrelated to spontaneous foetal reduction event but to effect of multiple foetuses on pregnancy and inadequacies of intensive care units in the developing world.

INTRODUCTION

In Africa, infertility has remained a source of concern, due to its increasing prevalence, psychosocial consequences and inaccessibility to assisted conception treatment (1,2,3) Management of infertility in most African setting is at a crossroad due to controversies surrounding the allocation of scarce resources for treatment of common ailments that are mainly responsible for morbidities and mortalities in the tropics as against provision of capital intensive Assisted Reproductive Technology (ART) treatment for few that suffer immeasurably from psychological and social consequences of infertility(3, 4,5). Worldwide the incidence of multiple pregnancies has increased mainly as a consequence of ovarian stimulation and transfer of multiple embryos during assisted conception treatment (6). Women undergoing invitrofertilization treatment are exposed to higher rate of multifoetal pregnancies in the range 200-fold and 400-fold for twins and higher order multiple pregnancies respectively (7).

In most developed countries, there has been a consensual trend to de-emphasising pregnancy rate as a performance index of ART treatment due to threat to safety that may manifest in the form of ovarian hyper stimulation syndrome and increased perinatal morbidity and mortality associated with multiple pregnancies (8, 9). This has helped propagate the practise of elective single embryo transfer or at most two-embryo transfer. In contrast to what is obtainable in most developing countries where ART regulation is unavailable; multiple embryo transfer is the norm so as to increase the pregnancy rate in justification for the high financial commitment made by infertile couples to undergo ART treatment.

Studies have shown that super ovulation is associated with a

twenty percent incidence of twin pregnancy and about ten percent incidence for higher order multiple pregnancy (10, 11). Complications to both mother and foetuses are known to be significantly more with multiple pregnancies than singleton pregnancy. Ignorantly mindless of the medical, social and economic consequences, most patients in Africa see multiple pregnancies as a double joy. One of the unpreventable complications of multiple pregnancies is spontaneous foetal reduction otherwise known as vanishing foetal syndrome defined as first trimester missed abortion of one or more foetuses in a twin or higher order multiple pregnancies. The effect of vanishing foetus on ongoing pregnancy and immediate and remote foetal outcome is contentious. It was against this background that we studied maternofoetal outcome of multiple pregnancies that was complicated by spontaneous reduction among infertile women that had fertility treatment.

PATIENTS AND METHODS

This was a 5 year (July 2005 to June 2010) prospective observational study conducted in 2 public hospitals(Ahmadu Bello University Teaching Hospital, Zaria [ABUTHZ] and 345 Aero medical Hospital, Kaduna [345AMHK]) and 1 private hospital(Alba Clinics and Medical Centre ,Kaduna [ACMCK]) . All patients were evaluated for infertility before treatment. Patients conceived through non- ART treatment or were referred for ART treatment. Patients that underwent non-ART treatment had ovulation induction with 100 to 150mg of oral clomiphene citrate commenced on the second day of menstrual cycle, serial ultrasound follicular tracking from day 10 of menstrual cycle, stat dose of Human chorionic gonadotrophin injection(5000 to 10000 units) as soon as the dominant follicle(s) was at least 18mm and timed intercourse. Patients referred for ART all had invitrofertilization, intracytoplasmic sperm injection and embryo transfer.

All patients had early ultrasound scan and numbers of foetal heart beats documented before the spontaneous reduction episode. They were followed up taking into cognisance of any pregnancy complications and foetal outcome. In this study gestational age was calculated from the first day of the last menstruation or from the date of embryo transfer. Preterm delivery includes births before 37 completed weeks of gestation and early preterm delivery defined as births between 28 to 31 weeks. . Low birth weight includes babies that weighed less than 2.5kg while very low birth weight was defined as birth weight less than 1.5kg. Small for gestational age babies are babies with birth weight below the 10^{th} percentile of curves for singleton according to the gestational age at delivery.

RESULTS

Of the fifteen patients, 1 was managed in ABUTHZ, 2 at 345AMHK and the remaining 13 at ACMCK.. Fifteen pregnancies were managed, 9 (60%) were from non-ART conceptions and 6 (40%) from ART conceptions. All patients had treatment on account of secondary infertility. Maternal median age was 34 years with age range of 31 to 38 years. Aetiology of infertility were tubal occlusion (6 patients, 40%) and anovulatory disorders in 9 patients(60%). The 9 non – ART pregnancies were all twins spontaneously reduced to singletons, while the 6 ART pregnancies comprised of 4 (66.7%) twins reduced to singleton. 1 (16.7%) triplet reduced to twin and 1 quintuplet (16.7%) reduced to quadruplet. Overall after the spontaneous reduction there were 13(86.6%) singleton pregnancies, 1(6.7%) twin pregnancy and 1(6.7%) quadruplet pregnancy.

Outcome of 13 pregnancies reduced to singleton are pregnancy induced hypertension (3 patients, 23.1%), preterm delivery (1 patient, 7.7%), caesarean delivery (5 patients, 38.5%), postpartum haemorrhage (2 patients, 15.4%), low birth weight (2 babies, 15.4%), small for gestational age (2 babies, 15.4%) and macrosomia (1 baby, 7.7%). There was no perinatal or maternal death but 1 (7.7%) infant death due to complications of congenital heart disease was recorded.

The triplet pregnancy reduced to twin was complicated with severe hypertension in pregnancy and spontaneous abortion at 19 weeks. The patient with quintuplet pregnancy reduced to quadruplet had prophylactic cervical cerclage at 12 weeks but delivered at 7 months preceded by preterm premature rupture of membrane. Small for gestational age was recorded in 3(75%) of the 4 babies and all the 4(100%) babies were nursed in the neonatal intensive care unit. Three (75%) neonatal deaths were recorded due to hyaline membrane disease.

Figure 1

Table I: characteristcis of patients and pregnancies

AGE IN YEARS		
Median (range)	34	(31-38)
TYPE OF INFERTILITY (n=15)		
Secondary infertility	15	(100%)
AETIOLOGY OF INFERTILITY (n=15)		
Tubal Occlusion	6	(40%)
Anovulatory disorders	9	(60%)
TYPE OF TREATMENT AND MULTIPLE PREGNANCY		
ART (n=6)		
Twins		
Triplets	4	(66.7%)
Quintuplet	1	(16.7%)
Non – ART (n=9)	1	(16.7%)
Twins	9	(100%)
TYPE OF PRGENNACY AFTER SPONTANEOUS		
REDUCTION (n=15)		
Singleton	13	(86.6%)
Twins	1	(6.7%)
Quadruplet	1	(6.7%)

Figure 2

Table II: outcome after spontanoeus reduction

SINGLETON	N=13	%
Pre-eclampsia / Eclampsia	1	7.7%
Preeterm delivery	1	7.7%
Caesarean delivery	5	38.5%
Postpartum haemorrhage	2	15.4%
Low birth weight	2	15.4%
Small – for – gestation	2	15.4%
Macrosomia	1	7.7%
New Admission	3	23.1%
Congenital heart death	1	7.7%
Prenatal death	0	0.0%
Maternal death	0	0.0%
Infant death	1	7.7%
TWIN	N = 1	%
Pre-eclampsia	1	100.0%
Miscarriage	1	100.0%
QUADRUPLET		%
PPROM (n = 1)	1	100.0%
Early preterm delivery (n = 1)	1	100.0%
Very low birth weight (n = 4)	4	100/0%
Small for gestation (n = 4)	3	75.0%
NICU admission (n = 4)	4	100/0%
Neonatal death (n = 4)	3	75.0%

PPROM – Preterm Premature Rupture of Membrane

NICU – Neonatal Intensive Care Unit

DISCUSSION

In Africa majority of pregnancies are unplanned and early ultrasound scan is not a routine. This study would not have been possible but for the fertility treatment that resulted in these pregnancies warranting early ultrasound confirmation. Studies have generally reported relatively poor pregnancy and foetal outcome associated with ART- conceived pregnancies compared to spontaneously conceived pregnancies (12, 13, 14). Some of the adverse outcomes are higher rates of operative deliveries, low birth weight, preterm births and neonatal morbidity and mortality. Postulated reasons for these adverse foetal outcomes may be the residual effects of spontaneous or iatrogenic foetal reduction on subsequent growth of the remaining foetus(15).In as much as there is no conclusive hypothesis on the aetiology of vanishing twin episode (VTE) , however chromosomal aberration of the vanishing foetus and infections are postulated aetiologies(15,16l).

The rate of singleton pregnancies following vanishing twin episode is said to be in the range of10.4 to 12.2%(17, 18) In twin pregnancies reduced to singletons, caesarean section and preterm delivery rates recorded in this series is similar to 32.6% and 19.6% respectively reported in a similar study(16) and in accord with another study that found no difference in the mean gestational age at delivery in normal singleton pregnancies and singleton pregnancies following vanishing twin episode(19) . However, when we compared the rates of early preterm delivery, low birth weight and small for gestational age with the same study (16), this series recorded lower rates for these adverse foetal outcomes. Although this might not be a fare comparison because Shebi's study involved patients who only conceived by ART (IVF/ICSI) while our series included non-ART assisted conceptions also. There is no balance of opinion on the outcome of pregnancies following vanishing twin episode. Authors have reported obstetrics and foetal indices that are similar to spontaneously conceived singleton pregnancies (17), while other studies recorded poorer outcome following vanishing twin episode (19, 20). In this study, there was no maternal and perinatal mortality recorded amongst singleton pregnancies following VTE which is comparable to finding from another study (16). Authors reported that spontaneously reduced singleton foetus from monozygotic twin may suffer higher adverse outcome than dizygotic twin, as a result of vascular anastomotic shunting anomalies(17) which is in consonance with the general trend in twins pregnancies conceived spontaneously(21). Other factors thought to be responsible for low birth weight as an adverse foetal outcome following ART conceived twin pregnancies are the number of embryo transferred, female factor infertility and fresh embryo transfer (22,23)

Spontaneous reduction in higher order multiple pregnancies

(HOMP) resulting in twin pregnancies is reported to occur in 36% of twin pregnancies (24). In this study, only two (13.3%) spontaneous reduction occurred in HOMP and resulted to a twin and quadruplet pregnancies, both were ART conceived pregnancies. The significantly high adverse pregnancy and foetal outcomes recorded for HOMP in this series underscore the practise of multiple embryo transfer and minuscule the ultimate benefits of ART treatment. Foetal outcome following spontaneous reduction in HOMP is associated with significantly poorer prognosis (25). More so in resource constrained settings of Africa, with inadequate neonatal intensive care management. Transfer of single embryo in ART treatment has been found to be associated with good foetal indices that are similar to outcomes in spontaneously conceived singleton pregnancies (26) and overwhelmingly better than double embryo transfer (27) not to talk of multiple embryo transfer.

From this series, pregnancy and foetal outcome in singleton pregnancies following VTE was good and comparable to similar study (17).However, another study recorded poorer foetal outcome (16). In the later study 60% of the study group presented with primary infertility while the entire patients in our series (100%) presented with secondary infertility. Could the type of infertility also have an impact on the ultimate foetal outcome even though this study was a small number series which is a constraint to reach a conclusion?

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