

Higher Order Multiple Births in Nigeria: Experiences, Challenges and Neonatal Outcomes in a Private Health Facility

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ABSTRACT

Objectives: The aim of this study is to describe the experience and outcome of higher order multiple (HOM) births in a private tertiary health facility in Nigeria. **Materials and Methods:** This was a retrospective review of records of HOM over 3 years in a private tertiary health facility in Nigeria. Relevant data on HOM births were extracted from both the patients' case notes, admission registers and maternity ward and delivery records of the hospital using a predesigned pro forma. Data were analyzed using Statistical Package for Social Sciences Version 22.0. **Results:** The prevalence of HOM births was 0.72% of 1950 births over the 3 years study period; while for triplets, quadruplets, and quintuplets were 0.56%, 0.1% and 0.05%, respectively. The mean gestational age was 32 ± 3 weeks, and all except three sets of triplets were by Assisted Reproductive Technology (ART). Respiratory distress syndrome, neonatal jaundice, and neonatal sepsis accounted for more than 80% of the neonatal complications noted in HOM births. However, there was no significant difference between neonatal survival of HOM as compared to twin deliveries, *P* = 0.08. **Conclusion:** HOM is becoming increasingly common in Nigeria. The strongest risk factor is ART, and neonatal complications are common reinforcing the need to streamline ART protocols in Nigeria.

KEYWORDS: Higher order multiple births, neonatal outcome, Nigeria, private health facility

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INTRODUCTION

Higher order multiple (HOM) births are deliveries of three or more babies in one pregnancy. Once a rarity, these deliveries are now seen more frequently in Nigeria due to the advent of fertility treatments and advanced maternal age at conception. Studies have shown that HOM births are associated with Assisted Reproductive Technologies (ARTs), and the proportion of multiple births after therapy is consistent regardless of the method used.^[1,2] The prevalence of HOM pregnancies and deliveries in the USA increased 4–8 folds a decade ago^[3] with 40% of the births resulting from ovulation induction, 40% from ART, such as *in vitro* fertilization (IVF) with embryo transfer, intracytoplasmic sperm injection, and intra-tubal transfer of gamete or zygote.^[4,5] The remaining 20% of HOM pregnancies occur spontaneously.^[6,7] In recent times, however, developed countries such as the USA and

Europe are now frowning at HOM pregnancies. Due to ethical issues regarding HOM births arising from ART, the trend now is to reduce the incidence of HOM births by reducing the number of embryos transferred.^[3]

In Nigeria like other developing countries, ART is beginning to gain ground after a previous delay in availability of adequate facilities, high-cost implications of treatment, and some cultural beliefs in certain regions that multiple births are not normal and should not be accepted.^[8,9] The spontaneous occurrence of HOM births is rare. The natural incidence of triplets and quadruplets in Nigeria is 0.13%.^[9]

Triplet births occur in 0.2% of live births in Hausa women in Nigeria,^[10] whereas the Yorubas in the

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South-West are notable for the highest twinning rate in the world with four times as many twins and 16 times as many triplets as women from the US and Europe.^[11]

HOM births are associated with risks and complications with higher morbidity and mortality rates than singletons and twins.^[1] This is because they are usually born preterm and often of low birth weight (LBW)^[1,12] which raises the risk for increased morbidity and mortality. They are more prone to congenital malformations such as conjoined twins^[12] and cardiac defects^[10] in addition to problems of prematurity.

The socioeconomic and emotional demands that may accompany the birth of three or more premature babies at the same time tend to overwhelm the mother and her family, especially where family support is lacking or inadequate.^[13,14]

It was noted that most studies done on HOM births in Nigeria has been carried out in public hospitals.^[12,13] No study has documented the experience of the private sectors even though most of the advanced fertility centers in the country are owned by the private sector. There is need to ascertain the events which follow after fertility treatment. There is also need to ascertain the outcomes for these HOM birth babies in the private sector.

We aim to describe the experience of the Neonatal unit of a private tertiary health facility in Nigeria with the HOM births delivered in the hospital and the neonatal outcome over 3 years period (2012–2015).

MATERIALS AND METHODS

Our hospital is a private tertiary hospital with facility for advanced fertility treatment and neonatal care. It is a registered postgraduate training institution for Family medicine as well as Obstetrics and Gynaecology residents. The hospital is utilized by most Health Management Organizations (HMO) in Nigeria, and about 80% of the patients are enrolled in managed care. The hospital receives referrals from many HMOs and other private hospitals in Lagos for the management of their high-risk pregnancies and for neonatal care. The Special Care Baby Unit (SCBU) has six bed spaces with three incubators. There are two consultant paediatricians, family medicine resident doctors, and internship doctors rotating through paediatrics posting every 3 months.

Data on HOM births (triplets, quadruplets, and quintuplets) delivered at the hospital from April 2012 to March 2015 were retrospectively reviewed from the maternity ward and theater delivery registers and the SCBU admission register. Pregnancy delivered before 25 completed weeks of gestation were excluded from the study. Case notes of relevant infants were retrieved

and data collected on mother's bio data, gestational age, method of conception, mode of delivery, sex of the baby, birth weight, neonatal course, and morbidity patterns such as birth asphyxia, respiratory distress syndrome (RDS), sepsis, neonatal jaundice, and intraventricular hemorrhage. The neonatal outcome was also extracted (discharges, death, or referred). Information gathered was recorded into a predesigned pro forma.

Ethical approval was obtained from the hospital's Ethics and Research committee.

Data were analyzed using the Statistical Package for Social Sciences for Windows, version 22.0 (IBM Corp., Released 2013, Armonk, New York, USA). Frequency distributions and cross-tabulations for all variables were calculated as appropriate.

Demographic characteristics of the multiple birth mothers and the baseline characteristics of the HOM births were compared using Chi-square test. Student's *t*-test was used for continuous variables and Chi-square or Fisher's exact test was used to compare discrete variables. The level of significance was set at <0.05 at 95% confidence interval.

RESULTS

A total of 1950 deliveries with 2116 babies were recorded at the hospital within the 3 years study period, of which sixty were sets of twins (114 live babies and 6 stillbirths) and 14 were sets of HOM births (46 babies). The HOM births comprised of 1 set of quintuplets, 2 sets of quadruplets, and 11 sets of triplets.

The prevalence of HOM births was 14 (0.72%) of 1950 births over the 3 years study period; while for triplets, quadruplets, and quintuplets were 0.56%, 0.1%, and 0.05%, respectively. The mean maternal age of the HOM births was 34.35 ± 5.5 years. The maternal demographic characteristics of the HOM and twin births are shown in Table 1.

Only three sets of triplets out of the 14 sets of HOM births were not IVF conceptions. Twelve sets of the HOM births were delivered by cesarean sections. The other two sets (triplets) were delivered vaginally. The indications for the cesarean deliveries, in addition to being high risk pregnancies included: Preterm labor in 5 (41.6%) of the 12 mothers sectioned, severe preeclampsia in 4 (33.3%), antepartum hemorrhage in 1 (8.3%), preterm prolonged rupture of membranes in 1 (8.3%), and active hepatitis in one mother (8.3%).

Table 2 shows the baseline characteristics of the HOM births. All the HOM births were preterm, and all were admitted to the special baby care unit of the hospital.

The mean gestational age of the HOM was 32 ± 3 weeks with a mean birth weight of 1765 ± 590 g. Both sets of quadruplets were of the late preterm category, the quintuplets were moderate preterm. Among the triplets, two sets were extreme preterm, one set was early preterm, and another two sets were moderate preterm, whereas six sets of

triplets were of the late preterm category. The birth weight category was also shown.

Figure 1 shows the major neonatal complications noted in the HOM births. Respiratory distress syndrome

Table 1: Demographic characteristics of the multiple birth mothers

Parameter	HOM (n=46)	Twins (n=114)	P
Mean age (years)	34.4±5.5	32±5.5	0.02
Parity, n (%)			
1	15 (32.6)	51 (44.7)	0.002
2	22 (47.8)	20 (17.5)	
3	6 (13.0)	32 (28.1)	
4	3 (6.5)	5 (4.4)	
>4	0	6 (5.3)	
Mode of delivery and number of babies (%)			
Caesarean section	40 (87.0)	95 (83.3)	0.568
Vaginal delivery	6 (13.0)	19 (16.7)	

HOM=Higher order multiple

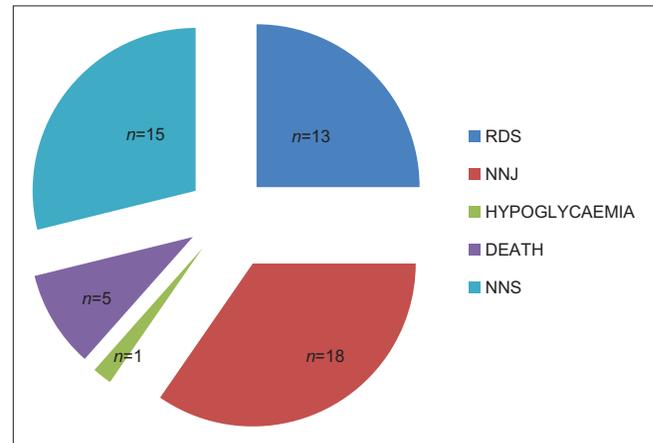


Figure 1: Major neonatal complications noted in higher order multiple births. n=number of babies. Some babies had more than one complication; RDS=Respiratory distress syndrome; NNJ=Neonatal jaundice; NNS=Neonatal sepsis

Table 2: Baseline characteristics of the higher order multiple birth newborns

Parameter	Triplets, n (%)	Quadruplets, n (%)	Quintuplets, n (%)	P
Mean gestational age (weeks)	32.45±3.6	34.0±0.00	33.0±3.1	0.24
Gestational age range (weeks)	25-36	34	33	
Mean birth weight (g)	1684±588	2236±569	1540±115	0.04
Birth weight category				
LBW	21	8	3	
VLBW	6	0	2	
ELBW	4	0	0	
NBW	2	0	0	
Sex				
Male	10 (30.3)	4 (50)	3 (60)	0.31
Female	23 (69.7)	4 (50)	2 (40)	
Mode of delivery and number of babies				
Caesarean section	27 (81.8)	8 (100)	5 (100)	0.26
Vaginal delivery	6 (18.2)	0	0	

LBW=Low birth weight; VLBW=Very low birth weight; ELBW=Extremely low birth weight; NBW=Normal birth weight

Table 3: Neonatal outcome of higher order multiple births compared with twin births

Parameter	HOM (n=46)	Twins (n=120)	P
Mean gestational age (weeks)	32±3	34±3	0.0002
Mean birth weight (g)	1765±589	2318±558	0.0002
Range of birth weight (g)	500-3540	700-3180	
Sex			
Male	17 (37.0)	51 (44.7)	0.38
Female	29 (63.0)	63 (55.3)	
Neonatal survival	41 (89.1)	107 (89.2)	0.08
Stillbirth	0	6	0.18
Length of hospital stay (days)	11±8	6±5	0.0001
Perinatal mortality rate	108.7/1000 live HOM birth	108.3/1000 live twin birth	

HOM=Higher order multiple

(RDS), neonatal sepsis, and neonatal jaundice together account for more than 80% of the morbidities seen in these babies.

Table 3 shows that of the 46 HOM, 41 survived with 5 deaths; and of the 114 live born twins, 107 survived with 7 deaths making a total of 12 neonatal deaths in babies of multiple gestations. There was no stillbirth recorded in the HOM, but there were 6 stillbirths recorded in the twin deliveries during the study period.

RDS caused four of the five mortalities recorded for HOM births and sepsis in one. RDS and neonatal sepsis were the major causes in twin deaths with three dying from RDS and another three from complications of neonatal sepsis. During the study period there were overall, thirty-six neonatal deaths out of the 2116 live births recorded over the period giving a neonatal mortality rate of 17/1000 live births. Thirty of the neonatal mortalities were in preterm babies, five of which occurred in HOM, seven in twins' and 18 in singletons preterm. The remaining six neonatal deaths occurred in singleton term neonates. Among the five mortalities in HOM three occurred in nine of the triplets with gestational age <30 weeks.

DISCUSSION

The prevalence of HOM birth in this study is very high at 0.74% compared to other studies reported in Nigeria.^[12,13] It is also higher than the 0.11% prevalence documented by Martin *et al.* in the USA.^[15] Fajolu *et al.*^[12] reported a prevalence of 0.32% at a tertiary hospital in South-West Nigeria, whereas Umeora *et al.*^[13] in South-East Nigeria reported a prevalence of 0.13% at the two facilities studied. The apparent increase seen in the present study may reflect the fact that all the subjects reported underwent fertility treatment at the index hospital. Nearly all the HOM are IVF conceptions. The other studies^[12,13] probably reported high-risk HOM that were referred to their facility for delivery as Fajolu *et al.* reported almost 40% of the deliveries as being unbooked.^[12] The tendency to want to be followed up and delivered in a facility where the pregnancy was achieved is a natural one.

Mothers who delivered HOM births were significantly older than those who delivered twins ($P = 0.02$). This was noted in the study by Umeora *et al.*^[13] The changing trend of women pursuing careers earlier in life and starting family late, predispose to increase in infertility issues; hence, the greater need for ART in older mothers. The later is more likely to be financially independent and can afford the economic burden of ART. In our culture, couples try spontaneous conception for years before seeking assistance even when they have known factors militating against spontaneous conception.

All the HOM births in this study were delivered preterm. This reiterates the earlier findings by Mazhar *et al.*^[16] in Pakistan that women with multiple gestations are at increased risk for preterm labor. They also have a higher risk for pre-eclampsia and antepartum hemorrhage, all which can lead to preterm delivery.^[17,18] These complications were all exhibited in the present study.

The mean gestational age of 32 weeks in the present study is similar to 32.6 weeks documented in South-East Nigeria by Umeora *et al.*^[13] The gestational age at birth determines the relative maturity of the infant. The lower the gestational age, the more premature the physical and functional capability of the infant. Hence, gestational age and birth weight are the two most important determinants for perinatal morbidity and mortality. The mode of delivery may also confer a protective benefit to these high-risk newborns. All (87%), except six of the HOM births in the present study, were delivered by cesarean sections and three of the vaginal deliveries died. This is similar to the 89% cesarean sections reported by Collins and Bleyl^[17] in quadruplet's deliveries. Fajolu *et al.*^[12] also reported that most of their HOM pregnancies were delivered by cesarean sections (82%) and they recorded no mortality in babies of those offered elective cesarean sections. The cesarean route may be a less stressful route of delivery for HOM births that are most often preterm.

The mean birth weight of the HOM in the present study was 1765 ± 589 g being lowest (1540 ± 115 g) in quintuplets and highest (2236 ± 569 g) in quadruplets. This is different from the report from other studies that found triplets to have higher weights than quadruplets. This may be explained by the lower number of quadruplets in the present study and also that these quadruplets were relatively of higher gestational age. In the study by Collin and Bleyl,^[17] the mean birth weight of quadruplets was 1482 g. The LBW noted in all the HOM in the present study placed them at risk of all the problems of LBW babies in addition to prematurity.

The neonatal outcome in this study is better than previously reported by other authors.^[19] In our cohort, the mean duration of hospital stay for HOM was shorter than that reported by Seoud *et al.* in Norfolk.^[19] This may be explained by the higher mean gestational age and mean birth weight seen in our participants. The neonatal survival was comparable to those seen in twin deliveries, and it is not statistically significant ($P = 0.08$). Infant survival increased with gestational age and was worse for gestational ages <30 weeks with 33% mortality. This is similar to the study by Yudin and Asztalos^[20] that documented high survival rate (>90%) in higher gestational age infant of HOM. Infants born at the lower limit of viability have the highest mortality

