Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2017, 6(6): 166-170

Fetomaternal Outcome in Triplet and Quadruplet Pregnancies: A Retrospective Study

Maasoumeh Mirzamoradi[1], Zahra Heidar[2], Maasoumeh Saleh[3*]

[1] Assistant Professor of Perinatology, Mahdiyeh Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[2] Assistant Professor of Infertility, Mahdiyeh Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[3] Department of Gynecology and Obstetrics, Shahid Beheshti University of Medical Sciences, Tehran, Iran

**Corresponding e-mail: salehmaasoumeh@yahoo.com*

ABSTRACT

Background: *In recent decades, there has been a dramatic increase in the prevalence of multiple pregnancies. An important reason is the increased use of assisted reproductive techniques for conception. Despite the advances in prenatal care, maternal and neonatal morbidity and mortality caused by multiple pregnancies are still high.* ***Aim:*** *This study aimed to evaluate the fetomaternal complications in higher order multiple pregnancies.* ***Design:*** *The design is a retrospective study.* ***Setting:*** *Triplet and quadruplet pregnancies were investigated in this study.* ***Methods:*** *This study investigated the outcome of triplet and quadruplet pregnancies born alive at the Mahdiyeh hospital, Tehran, Iran from 2006 to 2015.* ***Results:*** *In this study, 111 triplet pregnancies and 24 quadruplet pregnancies were studied, 80% of which resulted from assisted reproductive technology. The average age of pregnancy termination was 31 weeks, the average weight of the first to third neonates was 1400 g and the average weight of the fourth neonate was 700 g. The most common reason for early termination of pregnancy was preterm labor, the most maternal complication was uterine atony and the most common neonatal complication was pre-maturity and then respiratory distress syndrome (RDS). The mean age of mother in triplets' deliveries was significantly lower than in the quadruplets. The average weight of the first to third neonates, the average of 1st and 5th minutes Apgar score of the first neonates and the average gestational age of termination for the first and second neonates in triplets was significantly higher than in the quadruplets. Hospitalization due to preterm labor in quadruplets' delivery was significantly higher than in triplets.* ***Conclusion:*** *Higher order multiple pregnancies are associated with higher maternal and neonatal complications. Mothers with such pregnancies needs more care in the prenatal period, during labor and in the postpartum period, and also their neonates need more care after birth, most commonly due to prematurity.*

Keywords: Triplet and quadruplet pregnancies, Fetomaternal complications, Prematurity

INTRODUCTION

The incidence of multiple births has risen in the last 30 years [1]. Two important factors associated with this are the tendency towards increased maternal age, which may be associated with higher rates of spontaneous multiple births [2], and the increasing use of medical assistance for conception [3,4].

Multiple pregnancy is associated with higher risks for both the mother and babies [1]. Women with multiple pregnancies have an increased risk of miscarriage, anaemia, hypertensive disorders, haemorrhage, operative delivery, and postnatal illness [1]. Neonatal complications include: perinatal mortality, respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), chronic lung disease, intracranial haemorrhage (ICH), retinopathy of prematurity (ROP), pneumothorax, patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC), hydrocephalous and congenital anomalies [5]. Preterm delivery is the most significant complication of triplet gestation, with approximately 75% to 100% of triplets being born prematurely [6].

Neonatal complications are mainly attributable to extreme prematurity and intrauterine growth restriction (IUGR) [7]. The significantly higher preterm delivery rates in multiple pregnancies imply that there is increased demand for specialist neonatal resources [1]. Due to the increased risk of complications, women with multiple pregnancies require more monitoring and increased contact with healthcare professionals during their pregnancy than women with singleton pregnancies [1].

The combination of growing number of triplet and quadruplet pregnancies and the potential for problems facilitated the need and importance of the present study. The role played by infertility treatment methods in the high incidence of multiple births resulted to the adoption of a more restrictive policy for reproductive medicine by many countries, setting for example the highest limit of transferred embryos at two [8]. In countries applying such a strong policy, this has shown to be effective, as demonstrated by Robert et al. [9] who discovered no significant increase in higher order multiple pregnancies in New South Wales, Australia during the last decade [8].

The reduction in multiple pregnancy is a widespread therapy to diminish the risk of prematurity and adverse outcome for the survivors in high order multiple gestation [5]. Multifetal pregnancy reduction (feticide) is ethically problematic and difficult to accept for some patients and therefore should not be part of a routine (infertility) treatment planning [5].

METHODS

In this study which was conducted from the beginning of 2013 to the end of 2015, the data of 135 pregnancies inclusive triplets and quadruplets at a Tertiary Obstetric Referral Center, Mahdiyeh Hospital, were used. For this study, triplet and quadruplet pregnancies were defined as a pregnancy that began 20 weeks, leading to the registration of at least one birth. In this study, the number of triplets and quadruplets reduced to twins was ignored. Data were collected by designed sheets, including maternal and neonatal information according to the documents of each mother and neonates by a resident. Exclusion criteria included: incomplete documents of mothers or neonates and induced abortion of higher order multiple pregnancies. Finally, maternal, and neonatal data were analyzed. For the comparison of quantitative variables between triplet and quadruplet pregnancies, independent t-test (for normally distributed variables) and Mann-Whitney test (for variables without normal distribution) were used, and for comparison of qualitative variables, chi-square test (for variables with chi-square test assumptions) and Fisher's exact test (for variables without chi-square assumptions) were used.

RESULTS

In this study, 135 women were studied, 111 women (82/2%) had triplet pregnancy and 24 cases (17/8%) had quadruplet pregnancy. The results of these pregnancies were 333 triplet foetuses which led to the birth of 325 live babies and 96 quadruplet foetuses which led to birth of 95 live babies (the total number of live-born babies = 420).

With regards to the average age, the sample was quite young (average age = 28) and the average body mass indexes based on standard guidelines corresponded with the overweight group (mean 28). The average gestational age of termination was 31 weeks, the average weight of the first neonate to third was 1400 g and the average weight of fourth neonate was 700 g. The mean gestational age and birth weight, respectively in the triplet pregnancy was 33 weeks and 4 days and 1557 g, and in quadruplets it was 28 weeks and 1 day and 1056 g. The Apgar score of all neonates except the fourth ones in both measurements (first and fifth minutes) was 8 and average score of Apgar score in fourth neonate in first measurement (first minute) was 6 and in second measurement (five minutes) it was taken as 7. The mean duration of hospitalization in surviving neonates in triplets was 22 days and in quadruplets was 31 days.

This study demonstrated that 99% of neonates were under 37 weeks (preterm), among which 71.1 percent were under 34 weeks and 16.3% were under 28 weeks. The weight of neonates at birth in the first neonates in 97%, second neonates in 96.3%, and the third neonates in 97% and fourth neonates in 100% was below 2500 g (low birth weight), this continued in 51.5, 51.7, 60.4 and 97.8% of neonates with weight below 1500 g (very low birth weight). Thus, the percentage of neonates between 1500 g and 2500 g (low birth weight) were, respectively, 45.5, 44.6, 36.6 and 2.2%.

The majority of subjects were without any history of stillbirth, had history of infertility, no children, no previous pregnancy history, no history of abortion, ectopic pregnancy and preterm birth. 81.5% of women in this study had a history of infertility, and the majority (80%) became pregnant with assisted reproductive technology (ART). Except for one case, none of the individuals had experience of drug abuse.

The experience of Cerclage was negative in more than half of the subjects surveyed (44.4% had cerclage). The use of progesterone was positive in majority of the subjects (55.6%), and among consumers the intravaginal form (cyclogest)

was more common than the systemic form (proluton). Majority of the subjects had received at least one course of betamethasone (73% 1 course and 2% two courses), thus a total of 75% received betamethasone.

The results of this study demonstrated that majority of women (66%) experienced complications as follows: 24% uterine atony of which one case led to hysterectomy, 23% preeclampsia of which one case led to HELLP, 11% gestational diabetes, 5% anaemia, 2.9% blood transfusion after uterine atony.

Separately, 65% of triplet pregnancies and 71% of quadruplet pregnancies in this study were experiencing maternal complications.

Preterm labor without rupture of membrane (ROM) was observed in 62 cases of triplet pregnancies (55.8%) and 11 cases of quadruplets (45.8%), and premature rupture of membranes (ROM) was observed in 39 cases of triplet pregnancies (35.1%) and 8 cases of quadruplets (33.3%).

Foetal complications were present in 66% of neonates which are discussed as follows:

1) Respiratory distress syndrome (RDS): this was observed in 134 neonates (41.2%) result of triplet pregnancies and in 33 neonates (34.7%) result of quadruplets.

2) Hyperbillirubinemia: this was observed in 131 neonates (40.3%) result of triplet pregnancies and in 22 neonates (23%) result of quadruplets.

3) Intrauterine growth retardation: this was observed in 75 neonates (17.8%) (17% triplet and 20% quadruplets).

4) Perinatal mortality: this was observed in 9 cases of intrauterine deaths and 32 cases of death after birth (total of 41 neonates, 9.7%).

5) Congenital anomalies in 24 neonates (5.7%): The most common is patent foramen ovale (PFO) which was observed in 7 neonates (29%), and then atrial septal defect (ASD) observed in 4 neonates (16%), ventricular septal defect (VSD) observed in 3 neonates, cleft lip and cryptorchidism observed in 2 neonates, oesophageal atresia, polydactyly, tracheoesophageal fistula (TEF), ureteropelvic junction (UPJ) obstruction, anencephaly and holoprosencephaly in 1 neonate.

6) Patent ductus arteriosus (PDA): this was observed in 14 neonates (3.3%).

7) Sepsis, retinopathy of prematurity (ROP): Each observed in 6 cases (1.4%).

8) Hydrocephalous: this was observed in 5 cases (1.1%).

9) Pulmonary HTN: this was observed in 4 cases (0.95%).

10) Cerebral palsy (CP): this was observed in 3 neonates (0.7%).

11) Pneumothorax, bronchopulmonary dysplasia (BPD) and necrotizing enterocolitis (NEC): each observed in 2 cases (0.47%).

In this study, four pregnancies were associated with placental abruption complication, 4 with chorioamnionitis and two neonates had acidosis at birth time (pH less than 7).

To compare the quantitative variables between women delivered triplets and women delivered quadruplets, independent t-test (for normally distributed variables) and Mann-Whitney test (for variables without normal distribution) were used. The results of these tests are as follows: The mean age of mother in triplet deliveries was significantly lower than the mean age of quadruplets; the mean weight of the first to third neonates, the mean score of one and fifth minutes Apgar score of the first neonates and the average gestational age of termination for the first in triplets and second neonates was significantly higher than the quadruples. Hospitalization due to preterm labor in quadruplets was significantly higher than triplets. In other variables, no significant difference was observed between the two groups.

DISCUSSION

In this study, the outcome of triplet and quadruplet pregnancies in 135 pregnant women (111 cases of triplet and 24 cases of quadruplets) and 420 neonates (325 cases result of triplet pregnancies and 95 cases result of the quadruplet pregnancies) between 2006 and 2015, in Mahdiyeh hospital, were studied. The average gestational age of termination was 31 weeks and mean birth weight in the first to third neonates was around 1400 g to 1500 g, and in the fourth neonate it was about 780 g. The mean gestational age and birth weight in this study, respectively in the triplet pregnancy was

33 weeks and 4 days and 1557 g, and in quadruplets it was 28 weeks and 1 day and 1056 g. About 50% of weight for gestational age of 33 to 34 weeks was between 1600 g to 1900 g and for 28 to 30 weeks it was 1000 g to 1300 g; such that the average weight of babies in the study in this period was less. In other studies, the average gestational age of termination of triplets was 33 to 32 weeks and in quadruplets it was 28 to 30 weeks, and the weight of neonates were 1900 g to 1600 g and 1100 g to 1000 g which when compared to this study, the weight and gestational age of triplets was less than other studies but in quadruplets, they were similar [10-14].

In this study, the most common neonatal complication after pre-maturity in first, second and fourth neonates was respiratory distress syndrome and in third neonates it was neonatal distress syndrome together with hyperbilirubinemia. Similar to results obtained in this study, pre-maturity and respiratory distress syndrome are the most common causes of morbidity in most studies [11,12].

Respiratory distress syndrome in this study in triplets was 41% and in quadruplets it was 34.7%. In some studies, RDS is significantly more in quadruplets than triplets and in some others; this is not different and is directly related to pre-maturity. This study also shows that neonatal complications are related to pre-maturity. In a study, Romaine Arlettaz et al. [12] in 2003 investigated 100 triplet and quadruplet pregnancies in Switzerland. A comparison between triplets and singletons was performed in similar gestational age, sex, and intervals (about the weight, complications, etc.), and none of these differences were significant. The result obtained confirms the theory that the morbidity and mortality of triplet and quadruplet pregnancies directly result from pre-maturity.

This study shows that low age of pregnancy termination and birth weight dramatically increases the rate of neonatal complications ($P<0.001$). In neonates weighing under 1500 g compared to neonates weighing between 1500 g and 2500 g as well, complications increased dramatically ($P<0.001$). The study shows that neonates with intrauterine growth retardation have significantly more complications ($P<0.001$) (chi-square test). The results of logistic regression in both receiving and not receiving betamethasone with an adjustment of the effect of gestational age, weight and intrauterine growth retardation showed that mothers who did not receive betamethasone were at risk of having neonate with respiratory distress syndrome at a level of 48% more than mothers who received betamethasone ($P=0.48$).

CONCLUSION

Finally, this study showed that the average weight of neonates and gestational age of triplet pregnancies were significantly higher than quadruplet pregnancies, but by eliminating the confounding factors (gestational age, birth weight, presence, or absence of intrauterine growth retardation, getting or not getting betamethasone), neonatal complication rate in the two types of pregnancy were not different and complications were directly related to pre-maturity. This result may suggest reduction as a strategy to reduce neonatal complications resulting from pre-maturity. In this study, regarding existence of only one case of reduction, we were unable to compare the complications. Between pregnancies with and without reduction, future studies will be dedicated to the comparison of neonatal complications in triplet pregnancies with and without reduction, but given the small numbers of these cases, more time will be required to carry out this study. This study showed that there were no differences between the gestational age of termination in women with and without cerclage and those with and without progestin; this result is similar to the findings in the study by Alexander Strauss et al. [10] in Germany in 2002.

According to incomplete data, in this study we were unable to compare the effect of cerclage on gestational age of termination in women with short and normal cervical length. Due to the lack of effectiveness of these methods to prevent preterm delivery, limiting the methods of infertility, appropriate advice to people before conception and reduction should be considered as the only remaining methods.

This study showed that the rate of respiratory distress syndrome (with removal of gestational age, birth weight, and intrauterine growth retardation) was lower than neonates whose mothers received betamethasone routinely than babies whose mothers did not receive betamethasone. This result may suggest the use of betamethasone routinely in this type of pregnancies in a particular gestational age, due to the high prevalence of pre-maturity in them. In the case of receiving one or two courses of betamethasone, in this study 73% of the neonates received one course and only two percent received two courses of betamethasone, so comparisons of these two were not done.

Finally, this study also similar to other studies, showed an increase in maternal and neonatal complications in higher order pregnancies and there is need for further studies on these complications due to the growing increase of this type of pregnancies and the need for special maternal, foetal and neonatal care. Also, according to the existing controversies in some mentioned cases, further studies can be helpful.

Key message points

Higher fetomaternal complications in higher order multiple pregnancies.

Consultation with infertile couples regarding the possibility of higher order multiple pregnancies and its complications before using assisted reproductive technologies.

REFERENCES

[1] Platt, Martin P. Ward, et al. "The North of England Multiple Pregnancy Register: Five-year results of data collection." *Twin Research and Human Genetics* 9.6 (2006): 913-918.

[2] Wood, R. "Trends in multiple births, 1938-1995." *Population Trends* 87 (1996): 29-35.

[3] The management of twin and triplet pregnancies in the antenatal period, September 2011, NICE clinical guidline 129.

[4] Malone, Fergal D., et al. "Maternal morbidity associated with triplet pregnancy." *American Journal of Perinatology* 15.01 (1998): 73-77.

[5] Devine, Patricia C., et al. "Maternal and neonatal outcome of 100 consecutive triplet pregnancies." *American Journal of Perinatology* 18.04 (2001): 225-236.

[6] Albrecht, Jan L., and Paul G. Tomich. "The maternal and neonatal outcome of triplet gestations." *American Journal of Obstetrics and Gynecology* 174.5 (1996): 1551-1556.

[7] Mastrobattista, Joan M., et al. "The rate of severe preeclampsia is increased in triplet as compared to twin gestations." *American Journal of Perinatology* 14.05 (1997): 263-265.

[8] Garite, Thomas J., et al. "Twins and triplets: the effect of plurality and growth on neonatal outcome compared with singleton infants." *American Journal of Obstetrics and Gynecology* 191.3 (2004): 700-707.

[9] Ho, Maw-Lin, et al. "Changing epidemiology of triplet pregnancy: etiology and outcome over twelve years." *American Journal of Perinatology* 13.05 (1996): 269-275.

[10] Strauss, Alexander, et al. "Multifetal gestation–maternal and perinatal outcome of 112 pregnancies." *Fetal Diagnosis and Therapy* 17.4 (2002): 209-217.

[11] Shinwell, E. S., et al. "Excess risk of mortality in very low birthweight triplets: a national, population based study." *Archives of Disease in Childhood-Fetal and Neonatal Edition* 88.1 (2003): F36-F40.

[12] Arlettaz, Romaine, Elena Paraskevopoulos, and Hans-Ulrich Bucher. "Triplets and quadruplets in Switzerland: comparison with singletons, and evolution over the last decade." *Journal of Perinatal Medicine* 31.3 (2003): 242-250.

[13] Adesiyun, A. G., and E. Eseigbe. "Triplet gestation: Clinical outcome of 14 cases." *Annals of African Medicine* 6.1 (2007): 12.

[14] Battin, Malcolm, et al. "Infant and perinatal outcomes of triplet pregnancy in Auckland: better than expected?." *The New Zealand Medical Journal (Online)*122.1298 (2009).