

Maternal and neonatal outcomes in twin and triplet gestations in Western Saudi Arabia

Samera F. AlBasri, MD, Ghadah M. Shouib, MD,
Osama S. Bajoub, MD, Hasan A. Nasrat, MD,
Ejaz Ahmad, MSc, Fahad M. AlGreisi, MD.

ABSTRACT

Objectives: To compare maternal and neonatal complications in twin and triplet gestations at King Abdulaziz University Hospital, Jeddah, Saudi Arabia.

Methods: Retrospective medical records of 165 women with 144 twin and 21 triplet pregnancies from 2004 to 2011 were analyzed. Comparisons were carried out for maternal complications, gestational age at birth, neonatal birth weight, and neonatal intensive care admission.

Results: Most common complications were preterm birth (49%), gestational diabetes mellitus (13.3%), and premature rupture of membrane (4.8%). All triplet pregnancies and 42% twin pregnancies terminated in preterm birth. Gestational length was longer ($p < 0.001$) in twin births (36.0 ± 3.05 weeks) than for triplet births (32 ± 3.81 weeks). Rates for in vitro fertilization, ovulation induction, and cesareans were higher in women with triplets than in those with twins. Neonatal intensive care unit (NICU) admission was higher ($p < 0.001$) for triplets (76.2%) than for twins (23.6%). The mean weight of twins was 2333.83 ± 558.69 grams and triplets was 1553.41 ± 569.73 grams. Hyaline membrane disease, neonatal jaundice, and neonatal sepsis were most common neonatal complications.

Conclusion: Neonates from triplet pregnancies were preterm, had low birth weight and needed more often NICU admission in comparison to those from twin pregnancies.

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Multiple gestation in women refers to a pregnancy when the mother carries 2 or more than 2 fetuses in her womb. The incidence of multiple gestations has increased substantially over the last 3 decades due to increased use of assisted reproductive technologies (ART) such as superovulation, in vitro fertilization (IVF), and

childbearing at older ages.¹ Multiple gestations are high risk pregnancies which may be complicated by maternal and neonatal morbidity and high neonatal and infant mortality.² Twins in comparison to singletons have 4-fold higher risk of death in pregnancy, 7-fold higher risk of death shortly after birth, 10-fold higher need for neonatal special care unit admission, and 6-fold higher risk of cerebral palsy.^{3,4} The risks for triplets are even higher. Multiple gestation also adversely predisposes the mother to gestational diabetes mellitus (GDM), pregnancy induced hypertension, miscarriage, anemia, preeclampsia, postpartum hemorrhage, intrauterine growth restriction of fetus, and fetal low birth weight resulting in greater neonatal morbidity and mortality.⁴ The risk of complications increases with the increase in the number of fetuses and the maternal age.

Preterm birth (PTB) is the leading direct cause of neonatal death (those occurring in the first 28 days of life) constituting approximately 27% of neonatal deaths worldwide with a total of one million deaths annually.⁵ Preterm twin deliveries contribute substantially to the overall PTB rates. In the United States and Canada, 10-14% of PTBs are twin deliveries.⁵ In 2014, neonates born in the United States to black parents had a 50% more risk of being born preterm than white, Hispanic and Asian neonates.⁶

The average duration of gestation for singletons is 39 weeks, for twins 35 weeks and for triplets 32 weeks.⁴ In the United States, birth data for the year 2006 indicated that almost all triplets (95%) were of low birth weight (<2500 g) and approximately 35% were of very low birth weight (<1500 g).⁷ In comparison, the rates for singletons were 6.5% and 1.1%, respectively. The emotional stress and complexity of caring for singleton newborns is significantly increased with multiple newborns.⁸ More than 25% of parents of multiple birth infants may have depression or anxiety disorders and experience a lower quality of life than parents of singletons.^{2,8}

Previously, a study on maternal and neonatal outcomes of high order gestations for the years 1985 to 2005 at King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia has been reported.³ However, twin pregnancies which form the major portion of multiple gestations were not included in the study. The aim of the present study was to compare the maternal and neonatal complications between twin and triplet gestations at the KAUH, Jeddah, using retrospective analyses of birth and clinical data between January 2004 and December 2011.

Methods. The current study is a retrospective cohort study utilizing the data for birth and clinical records at KAUH, Jeddah. Data for only twin and triplet pregnancies between January 2004 and December 2011 were included in this study. Monoamniotic-monochorionic twins and any gestations diagnosed with congenital malformations were excluded from this study.

Data for maternal complications, obstetrical complications, gestational age at birth, neonatal birth weight, Apgar score at 5 minutes, neonatal intensive care unit (NICU) admission, and neonatal complications were collected from the records. Gestational age at birth was based on the known date of conception, the date of embryo transfer or by first trimester ultrasonography. Preterm birth was defined as birth of an infant at less than 37 completed weeks of gestation. The diagnosis of pregnancy induced hypertension was made when blood pressure persisted at 140/90 mm Hg or greater after 20 weeks of gestation. The diagnosis of GDM was based on the results of oral glucose tolerance test. The Research Ethics Committee of the King Abdulaziz University approved the study and the study follows the principles of Helsinki Declaration.

Statistical analyses. Statistical analyses were performed using the Statistical package for Social sciences software version 17 (SPSS Inc, Chicago, IL, USA). Comparisons were carried out between twin and triplet pregnancies for age at birth, neonatal birth weight, Apgar score at 5 minutes and NICU admission. Chi-square test was employed to compare the proportional data between groups. For testing significant differences in discrete data between 2 groups, the independent t-test was carried out. A *p*-value <0.05 was set as the level of significance and data are presented as mean ± standard deviation.

Results. Retrospective analyses of the birth records between January 2004 and December 2011 showed

that a total of 42,980 deliveries occurred at KAUH. The number of multiple births was 212 (0.5%); prevalence of approximately 5 per 1000 births. The multiple births included 176 sets of twins, 29 sets of triplets, 6 sets of quadruplets and one set of quintuplets. However, only 165 women with 144 sets of twins and 21 sets of triplets were included in the current analyses. Most women were Asian (approximately 90%); 56.4% (n=93) were Saudi citizens, and 43.6% (n=72) were non-Saudi citizens. Most of women were multigravida (48.5%) followed by primigravida (31%), and grand multigravida (more than 5 pregnancies; 20.6%).

Preterm birth was the most common complication of multiple gestation with 60 twin pregnancies (42%) and all 21 triplet pregnancies (100%) terminating in PTB. Apart from PTB, combined for both types of multiple gestations, the most common obstetric complication was GDM in 22 pregnancies (13.3%) followed by premature rupture of membranes (PROM) in 8 pregnancies (4.8%). Most women did not have a history of maternal disease (83%) or any postpartum complications (96%) with no significant differences between women with twin and triplet pregnancies.

Cervical cerclage was carried out more often (*p*<0.001) in women with triplet pregnancies in comparison to women with twin pregnancies (Table 1). Combined for twin and triple gestations, cervical cerclage was more often (*p*<0.01) associated with PTBs. Gestational length was longer (*p*<0.001) in twin births (36.0 ± 3.05 weeks) than for triplet births (32 ± 3.81 weeks). Triplet pregnancies were more commonly (*p*<0.001) associated with the use of ART in comparison to twin pregnancies. The rate of cesarean section was 90% for triplet pregnancies compared to 63% of twin pregnancies.

A total of 144 twin pregnancies and 21 triplet pregnancies resulted in the delivery of 349 neonates with one vanished twin and one stillborn triplet.

Table 1 - Cervical cerclage and prematurity in women with triplet and twin pregnancies.

Variables	Cerclage		Total	χ^2	P-value
	No n (%)	Yes n (%)			
<i>Multi fetal gestations</i>					
Twin	139 (96.5)	5 (3.5)	144 (100.0)	43.22	<0.001
Triplet	11 (52.4)	10 (47.6)	21 (100.0)		
Total	150 (90.9)	15 (9.1)	165 (100.0)		
<i>Gestational age</i>					
<37	70 (85.4)	12 (14.6)	82 (100.0)	6.06	<0.014
≥37	80 (96.4)	3 (3.6)	83 (100.0)		
Total	150 (90.9)	15 (9.1)	165 (100.0)		

There were 11 neonatal deaths (8 for twins and 3 for triplets). Neonatal intensive care unit admission was higher ($p < 0.001$) for triplets (76.2%) than that for twins (23.6%; **Table 2**). The mean weight of twins was 2333.83 ± 558.69 grams and triplets was 1553.41 ± 569.73 grams. The mean Apgar score for twins (9.03 ± 1.49) was higher ($p < 0.04$) compared to that of triplets (8.29 ± 1.85). The percentage incidence of various neonatal complications is presented in **Table 3**. Hyaline membrane disease, neonatal jaundice and neonatal sepsis were common complications of prematurity.

Discussion. Multiple gestation is a significant medical risk for maternal and neonatal complications such as GDM, pregnancy induced hypertension, anemia, preeclampsia, postpartum hemorrhage, intrauterine growth restriction, low birth weight, PTB, and neonatal morbidity and mortality.^{1,2,4} The spontaneous prevalence of twins is one in 250 pregnancies (0.4%), triplets one in 10,000 pregnancies (0.01%) and higher order gestations one in 700,000 pregnancies (0.0001%).⁴ According to the United

States Department of Health and Human Services, the rate of twin pregnancies has shown more than 75% increase since 1980 and the rates of higher order multiple gestations even a higher increase.⁴ The increase has been attributed to the use of infertility treatments and more women delaying pregnancy until later in life.⁹ Globally, 45% of pregnancies resulting through IVF are multiple gestations.⁹

In the present study, the percentage of multiple gestations was 0.5% which is a prevalence of approximately 5 per 1000. Further breakup shows prevalence of twins 4 per 1000, triplets approximately 7 per 10000 and higher order gestations about 2 per 10000. The prevalence of twins was similar to that reported in earlier studies;^{4,9} however, the prevalence is lower than that reported from Armed Forces Hospital and King Khalid University Hospital, Riyadh (14 per 1000).¹⁰ The prevalence of triplets and higher order gestations was on higher side compared to previous reports;⁴ however, the prevalence was similar to that reported (6 per 10000 and one per 10000, respectively) from the same hospital for the years from 1985 to 2005.³ Higher prevalence of triplets compared to reported spontaneous prevalence

Table 2 - Neonatal intensive care unit (NICU) admissions and neonatal deaths in twins and triplets.

Variables	Multifetal gestations		Total	χ^2	P-value
	Twin n (%)	Triplet n (%)			
<i>NICU</i>					
No	110 (95.7)	5 (4.3)	115 (100.0)	23.99	<0.001
Yes	34 (68.0)	16 (32.0)	50 (100.0)		
Total	144 (87.3)	21 (12.7)	165 (100.0)		
<i>Presence of death</i>					
No	136 (88.3)	18 (11.7)	154 (100.0)	2.25	0.134
Yes	8 (72.7)	3 (27.3)	11 (100.0)		
Total	144 (87.3)	21 (12.7)	165 (100.0)		

Table 3 - Percentage incidence of various neonatal complications of twins and triplets.

Neonatal outcome	Neonate 1 n=(165)	Neonate 2 n=(164)	Neonate 3 n=(21)
Respiratory distress	3.60	3.60	0.60
Hyaline membrane disease	7.90	7.30	3.60
Transient tachypnea of newborn	2.40	1.20	0.00
Neonatal jaundice	12.1	7.90	3.00
Neonatal sepsis	6.70	7.90	3.00
Necrotizing enterocolitis	1.20	2.40	0.00
Intraventricular hemorrhage	3.60	1.20	0.00
Patent ductus arteriosus	3.00	4.80	0.00
Neonatal death	4.80	4.80	1.80

is probably due to the inclusion of twin and triplet pregnancies from ART in the current study. The most common maternal complications in the present study were PTB, GDM, and PROM. Gestational diabetes mellitus and PROM were with similar incidence in twin and triplet pregnancies. Previously¹¹ in a large data set, higher frequencies of maternal complications were associated with triplet gestations. The absence of differences in the current study are not clear but smaller data set and women of different demographics may be reasons that differences were not found between twin and triplet gestation.

It is now known that cesarean section triplets have lower perinatal mortality and morbidity rates compared with vaginally delivered triplets.¹² For this reason, our obstetricians' consensus is to do cesarean section for triplets and higher-order pregnancies and that probably is the reason for higher cesarean section deliveries for triplets in the present study. The reported mean gestational age at birth was 35.8 weeks for twins and 32.5 weeks for triplets and the morbidity and mortality with multiple gestations was predominantly due to PTB.^{4,5} Our data showed similar results. Further, triplets were of smaller birth weight compared with twins even after adjustment for gestational age suggesting growth restriction among triplets. The perinatal mortality rate is 4 times higher for twins and 6 times higher for triplets compared to that of singletons due to prematurity and ensuing complications.^{2,4} In the present study, neonatal deaths occurred in 3 sets of triplets due to extremely very low birth weight (birth weight less than 1000 grams) and in 8 sets of twins due to prematurity. Single fetal death is common in early pregnancy and results in "vanishing twin syndrome".¹³ In our study, there was one case of a vanishing twin and the surviving twin did well after the delivery. The number and duration of NICU admissions increased with triplets as the neonatal birth weights and gestational ages decreased in our study. This was expected and similar to previous studies.⁵

Cervical cerclage in our data set did not reduce the risk of PTB as 80% of pregnancies with cerclage terminated in PTB. Previously, comparison of triplet pregnancies with and without cerclage in some studies showed similar rates of PTB at both less than 28 and 32 weeks while other studies with smaller number of pregnancies were equivocal.^{14,15}

Limitations of this study include retrospective nature of the study, small cohort of women available for analyses especially for women with triplets, inclusion of both spontaneous and ART pregnancies in the analyses,

and inclusion of women of different demographics in the analyses. In view of the adverse effects of multiple gestations on maternal and neonatal outcomes, prevention of high-order multiple pregnancies should be the primary objective. Success of such initiatives is dependent on the prediction of excessive ovulation in infertility treatments and restrictions on embryo transfer for ART procedures. When these practices are followed, approaches such as ultrasound monitoring of ovulation induction and superovulation intrauterine insemination cycles with cancellation or transfer to IVF have been shown to markedly reduce the high-order multiple birth rate without significantly reducing the pregnancy rate.

In conclusion, our study on the maternal and neonatal outcome of twin and triplet pregnancies at KAUH, Jeddah indicates that the triplet pregnancies have a higher risk of PTB than twin pregnancies. Gestational diabetes mellitus and PROM were other main maternal complications but had similar incidence in twin and triplet gestations. Cervical cerclage did not improve the risk of PTB. Neonates from triplet pregnancies were of shorter gestational age, low birth weight, and needed more often NICU admission in comparison to that from twin pregnancies.

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From the Department of Obstetrics and Gynecology (AlBasri, Shouib, Bajouh, Nasrat), King Abdulaziz University Hospital, the Department of Fundamental and Applied Biology (Ahmad) King Fahd Medical Research Center, King Abdulaziz University, Jeddah, and the Department of Obstetrics and Gynecology (AlGreisi), King Abdullah Medical City, Makkah, Kingdom of Saudi Arabia. Address correspondence and reprints request to: Dr. Samera F. AlBasri, Department of Obstetrics and Gynecology, College of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia. E-mail: salbasri@kau.edu.sa
ORCID ID: <http://orcid.org/0000-0003-3019-1621>

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