

Maternal morbidity and infant death in twin vs triplet and quadruplet pregnancies

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BACKGROUND AND OBJECTIVE

In 2004, 139,494 infants were born of multiple pregnancies in the United States, which included 132,219 twins, 6750 triplets, 439 quadruplets, and 86 quintuplets and higher-order multiples. In the United States and many other industrialized nations, the number of multiple births has risen dramatically over the past 3 decades, mainly because of the increasing use of fertility therapies and assisted reproductive technologies (ART). Infertility affects an estimated 15% of women.

The use of ART carries a risk for multifetal pregnancy that ranges from 30%-50%, depending on the medications and techniques that are used. According to 2003 clinic data from the Society for Assisted Reproductive Technology, approximately 35% of ART pregnancies (29% twins, 6% triplets) and approximately 34% of ART births (31% twins,

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OVERVIEW

Maternal factors may be important in reducing the excess likelihood of complications in triplet and quadruplet vs twin pregnancies and include a 4- to 8-fold increased risk for birth at <29 weeks of gestation and a 3- to 4-fold increased risk for infant death, respectively.

3% triplets) were multiples. The twin and triplet or higher-order multiple rates for pregnancies that are conceived by ART are estimated to be 14-fold and 54-fold higher, respectively, than for the country as a whole.

ART alone is estimated to account for 44% of triplets and 16% of twins who were born in 2003. Triplets remain the focus of controversy regarding multifetal pregnancy reduction; some studies suggest that better outcomes occur when triplets are reduced to twins, although other studies report comparable outcomes when triplets are not reduced.

The purpose of this study was to calculate nationally representative, population-based estimates of maternal and neonatal risks in triplet and quadruplet pregnancies compared with those of twin pregnancies.

MATERIALS AND METHODS

We accessed data for 1995 through 2000 from the Matched Multiple Birth Data Set, National Center for Health Statistics, which includes maternal and pregnancy-specific data on all twin, triplet, and quadruplet live births at ≥ 20 weeks of gestation.

We defined maternal morbidity as selected medical risk factors that were present before or during pregnancy and complications of labor and delivery, birth at <29 weeks of gestation, and infant death of ≥ 1 babies. Each of these factors was calculated individually as a

percentage of plural births and modeled as the Mantel-Haenszel odds ratio and 95% CI, with results adjusted for maternal age, race and ethnicity, parity, and smoking status. The Table lists the factors that were considered and presents our findings. The reference group was twins.

RESULTS

The study population included 316,696 twin, 12,193 triplet, and 778 quadruplet pregnancies. All maternal characteristics differed significantly across the 3 pluralities, with mothers of triplets and quadruplets more likely to be older, white, of lower parity, of higher education, non-smokers, and married. Compared with twins, mean gestation was 3.5 weeks shorter for triplets and 5.4 weeks shorter for quadruplets. Birth at < 29 weeks of gestation occurred in 5.6% of twin births, 16.9% of triplet births, and 28.3% of quadruplet births.

Risks that were significantly higher for both triplets and quadruplets compared with twins were diabetes mellitus (pregestational or gestational), pregnancy-associated hypertension, incompetent cervix, other medical risk factors, tocolysis, cesarean delivery, premature rupture of membranes, excessive bleeding during labor and delivery, other complications during labor and delivery, birth at < 29 weeks of gestation, and infant death.

COMMENT

Our results quantify the increase in risk with triplets and quadruplets vs twins, including the 4-fold and 8-fold increased risk for birth at < 29 weeks of gestation and the 3-fold and 4-fold increased risk for infant death, respectively. These findings are in line with our research on early childhood outcomes of twins vs triplets, with the latter having greater neonatal morbidity, lower mental and motor scores, slower postnatal growth, and



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TABLE

Comparison of medical risk factors and complications during pregnancy for triplets and quadruplets vs twins

Variable	Twins	Triplets	95% CI	P value	Quadruplets	95% CI	P value
	Adjusted odds ratio ^a	Adjusted odds ratio ^a			Adjusted odds ratio ^a		
Before pregnancy							
Cardiac disease	1.00	1.30	1.07-1.59	.009	1.31	0.63-2.72	.47
Acute or chronic lung disease	1.00	1.62	1.39-1.88	<.0001	0.81	0.37-1.79	.62
Renal disease	1.00	1.14	0.80-1.61	.46	1.59	0.54-4.68	.42
Genital herpes	1.00	0.68	0.53-0.88	.003	0.34	0.09-1.25	.11
Previous infant 4000+ g	1.00	0.74	0.57-0.96	.02	0.19	0.03-1.10	.07
Previous preterm or small-for-gestational-age infant	1.00	0.98	0.80-1.20	.86	0.61	0.23-1.57	.32
Before or during pregnancy							
Diabetes mellitus	1.00	1.64	1.51-1.78	<.0001	1.97	1.47-2.64	<.0001
Chronic hypertension (< 20 wk)	1.00	1.22	1.03-1.46	.02	1.04	0.50-2.17	.91
During pregnancy							
Anemia (Hct < 30/Hgb < 10)	1.00	1.33	1.20-1.48	<.0001	1.14	0.74-1.76	.55
Hydramnios/oligohydramnios	1.00	0.85	0.73-0.99	.04	0.53	0.25-1.10	.09
Pregnancy-associated hypertension	1.00	1.22	1.15-1.30	<.0001	1.27	1.00-1.61	.05
Eclampsia	1.00	1.69	1.46-1.94	<.0001	1.67	0.99-2.83	.05
Incompetent cervix	1.00	4.73	4.26-5.24	<.0001	9.46	7.22-12.39	<.0001
Rh sensitization	1.00	0.85	0.67-1.09	.21	0.77	0.30-2.00	.61
Uterine bleeding	1.00	1.48	1.26-1.74	<.0001	1.65	0.94-2.91	.08
Other medical risk factors	1.00	1.69	1.62-1.76	<.0001	2.40	2.06-2.80	<.0001
Obstetric procedures							
Amniocentesis	1.00	1.17	1.08-1.26	<.0001	0.97	0.71-1.32	.84
Ultrasound examination	1.00	1.05	1.00-1.10	.03	1.16	0.97-1.39	.11
Induction of labor	1.00	0.18	0.16-0.20	<.0001	0.12	0.07-0.20	<.0001
Stimulation of labor	1.00	0.24	0.22-0.27	<.0001	0.22	0.14-0.34	<.0001
Tocolysis	1.00	2.85	2.71-3.00	<.0001	5.03	4.27-5.91	<.0001
Cesarean delivery	1.00	6.55	6.15-6.97	<.0001	7.38	5.74-9.47	<.0001
Other obstetric procedures	1.00	1.12	1.05-1.20	.0008	1.04	0.80-1.35	.76
Complications of labor and delivery							
Febrile (> 100°F/38°C)	1.00	0.85	0.71-1.02	.08	1.31	0.76-2.26	.33
Meconium, moderate/heavy	1.00	0.68	0.56-0.84	.0003	0.58	0.25-1.36	.22
Premature rupture of membranes (> 12 hr)	1.00	1.53	1.43-1.64	<.0001	1.74	1.36-2.23	<.0001
Abruptio placenta	1.00	1.31	1.11-1.55	.001	1.34	0.72-2.48	.36
Placenta previa	1.00	1.34	1.05-1.70	.02	1.18	0.46-3.06	.74
Other excessive bleeding	1.00	1.50	1.29-1.73	<.0001	2.22	1.41-3.50	.0005
All excessive bleeding in labor and delivery ^b	1.00	1.41	1.27-1.56	<.0001	1.75	1.23-2.49	.002

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TABLE

Comparison of medical risk factors and complications during pregnancy for triplets and quadruplets vs twins

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Variable	Twins	Triplets			Quadruplets		
	Adjusted odds ratio ^a	Adjusted odds ratio ^a	95% CI	P value	Adjusted odds ratio ^a	95% CI	P value
Cord prolapse	1.00	0.70	0.50-0.97	.03	<i>1.19</i>	<i>0.46-3.09</i>	<i>.72</i>
Fetal distress	1.00	0.65	0.57-0.75	<.0001	<i>0.55</i>	<i>0.32-0.97</i>	<i>.04</i>
Other complications of labor and delivery	1.00	1.56	1.49-1.62	<.0001	1.77	1.51-2.07	<.0001
Early preterm birth and infant death							
Birth at < 29 weeks gestation	1.00	3.76	3.55-3.97	<.0001	7.96	6.71-9.44	<.0001
Infant death of ≥ 1 babies	1.00	3.02	2.77-3.29	<.0001	4.07	3.06-5.41	<.0001

Values in *italics* are based on small numbers (< 20 in the numerator or the denominator) and should be interpreted with caution.

^a Adjusted for maternal age, race, parity, and smoking status, with twins as the reference group.

^b Includes abruptio placenta, placenta previa, and other excessive bleeding during labor and delivery.

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more residual stunting, particularly of length and head circumference through early childhood.

Prevention of excess multiple births that are associated with ART has been advocated through recommendations to reduce the number of embryos that are transferred and to use single-embryo transfer in clinically appropriate patients. National guidelines have resulted in significant reductions in the number of embryos that are transferred and in the rates of higher-order multiple pregnancies.

Enhanced prenatal care has been shown to be effective in improving outcomes in multiples pregnancy, with targeted interventions for twins, triplets, and quadruplets. Elliott suggests that 4

primary nonmodifiable factors affect outcomes in higher-order multiple pregnancies: maternal height, parity (previous full-term, non-low-birthweight outcome), placentation, and number of fetuses. Maternal weight and age may also influence multiple pregnancy outcomes. Discordancy in crown-rump length and estimated fetal weight influences the rate of fetal growth and length of gestation, with mono chorionic placentation more than twice as likely to be associated with birthweight discordancy and significant differences in rates of fetal growth, which in turn are associated with very early preterm birth.

Adherence to weight gain guidelines is associated with optimal intrauterine growth, subsequent birthweight, and

longer gestation in singletons and twins. The adverse effects of smoking in multiple pregnancy have been well documented.

CLINICAL IMPLICATIONS

- National guidelines recommend reducing the number of embryos and transferring single embryos in clinically appropriate patients who undergo assisted reproduction.
- The primary nonmodifiable factors that influence outcomes in multiple pregnancies are maternal height, parity, placentation and chorionicity, and number of fetuses.
- The primary modifiable factor is maternal weight gain. ■