

## Gynaecology

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## FACTORS AFFECTING TIME OF SPONTANEOUS DELIVERY OF DICHORIONIC DIAMNIOTIC TWIN PREGNANCY



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### ABSTRACT.

Twin pregnancies pose a higher risk for intrapartum complications and perinatal morbidity and mortality. As more women delay childbearing and the number of pregnancies conceived with assisted reproductive technology rises, twins are becoming more common. However, uncertainties exist regarding the optimal gestational age and mode of delivery for twins. Obstetrical management decisions related to the delivery of twins ultimately focus on minimizing stillbirth and neonatal morbidity and mortality risks. Randomized controlled studies on these issues are unfortunately limited. Therefore, decisions on the delivery of twins must rely on the best available evidence. The question is about factors affecting the time of spontaneous delivery in dichorionic diamniotic twin pregnancy and what is the optimal gestational age for twin delivery. The objective of this study was to evaluate the association of the timing of delivering twins and the perinatal outcome, to minimize perinatal complication according to main determinant factor.

### Introduction

The incidence of twin pregnancy has shown a significant increase over the last several decades due to advanced maternal age and the development of assisted reproductive techniques. (1)

In those terms, it is evident that the twin birth rate increased from less than 2 percent of babies born in 1980 to over 3 percent of babies born in 2009. After 2009, the rate of increase did not continue to rise at the same pace. It remained stable and even slightly decreased from 2009-2012 to 33.1 per 1000 live births. (2)

Then, in 2014, it jumped slightly to a new high of 33.9 per 1000 live births. Keep in mind, however, that this number is calculated based on the number of overall births (singleton and multiple) in a given year. The actual number of twins was only slightly higher; as the overall number of births was actually lower. (3)

Twin fetuses usually result from fertilization of two separate ova—dizygotic or fraternal twins. Less often, twins arise from a single fertilized ovum that divides—monozygotic or identical twins. (4)

The outcome of the monozygotic twinning process depends on when division occurs. If zygotes divide within the first 72 hours after

fertilization, two embryos, two amnions, and two chorions develop, and a diamniotic, dichorionic twin pregnancy evolves. (5)

Two distinct placentas or a single, fused placenta may develop. If division occurs between the fourth and eighth day, a diamniotic, monochorionic twin pregnancy results. By approximately 8 days after fertilization, the chorion and the amnion have already differentiated, and division results in two embryos within a common amniotic sac, that is, a monoamniotic, monochorionic twin pregnancy. (6)

Twins of opposite sex are almost always dizygotic. Dizygotic twinning is much more common than monozygous splitting of a single oocyte, and its incidence is influenced by race, heredity, maternal age, parity, and, especially, fertility treatment. (7)

The risk for twin-specific complications varies in relation to zygosity as well as chorionicity — the number of chorions. The latter is the more important determinant. Specifically, there are increased rates of perinatal mortality and neurological injury in monochorionic diamniotic twins compared with dichorionic pairs. (5)

Chorionicity can sometimes be identified in the first trimester with sonography. Two separate placentas suggest dizygosity. In pregnancies with a single placental mass, it may be difficult to identify chorionicity. Identification of a thick dividing membrane generally 2 mm or greater — supports a presumed diagnosis of dichorionicity. (8)

Also, the twin peak sign is seen by examining the point of origin of the dividing membrane on the placental surface. The peak appears as a triangular projection of placental tissue extending a short distance between the layers of the dividing membrane. (9)

A carefully performed visual examination of the placenta and membranes after delivery serves to establish zygosity and chorionicity promptly in approximately two thirds of cases. The following systematic examination is recommended. (10)

If the neonates are of the same sex, blood typing of cord blood samples may be helpful. Different blood types confirm dizygosity, although demonstrating the same blood type in each fetus does not confirm monozygosity. (11)

Birth weights in twin infants closely paralleled those of singletons until 28 to 30 weeks' gestation. Thereafter, twin birth weights progressively lagged. Beginning at 35 to 36 weeks, twin birth

weights clearly diverge from those of singletons.(12)

More than five of every 10 twins and nine of 10 triplets born in the United States in 2010 were delivered preterm. (13)

Delivery before term is a major reason for increased neonatal morbidity and mortality rates in multifetal pregnancy. Prematurity is increased six fold and tenfold in twins and triplets, respectively in their review. (14)

Similar to singleton pregnancies, approximately 60 percent of preterm births in twins are indicated, about a third result from spontaneous labor, and 10 percent follow prematurely ruptured membranes. (15)

Single fetal death during late second and early third trimester presents the greatest risk to the surviving twin. Although the risks of subsequent death or neurological damage to the survivor are comparatively increased for monochorionic twins at this gestational age, the risk of preterm birth is equally increased in mono- and dichorionic twins. (16)

Regardless, unless there is a hostile intrauterine environment, the goal should be to prolong pregnancy. Timing of elective delivery after conservative management of a late second or early third trimester single fetal death is a matter of debate. Dichorionic twins can probably be safely delivered at term. (17)

Micronized progesterone administered vaginally to women with twins is of uncertain benefit. Cetingoz and coworkers gave 100 mg of micronized progesterone intravaginally daily from 24 to 34 weeks. These authors reported that this practice reduced rates of delivery before 37 weeks from 79 to 51 percent in 67 women with twins. (18)

Prophylactic cerclage has not been shown to improve perinatal outcome in women with multifetal pregnancies. Studies have included women who were not specially selected and those who were selected because of a shortened cervix that was identified sonographically. (19)

In the latter group, cerclage may actually worsen outcomes. (20) Administration of corticosteroids to stimulate fetal lung maturation has not been well studied in multifetal gestation. However, these drugs logically should be as beneficial for multiples as they are for singletons. (21)

If the first fetus is non vertex, cesarean delivery is typically performed, whereas cephalic-cephalic twins are commonly considered for vaginal delivery. (22)

Importantly, when comparing neonatal outcomes among all these options, second twins at term as a group have worse composite neonatal outcomes than those of their co-twin regardless of delivery method. (23)

**Materials and methods**

A prospective Cross-sectional study was conducted on 150 pregnant females in Alexandria University Maternity Hospital.

We examined of all eligible twin pregnancies attending at Elshatby Maternity University Hospital from January 2018 to August 2018, and all those babies delivered. Co-twin deaths are excluded.

Maternal and perinatal data had been obtained from mothers and medical records to evaluate the relation between the timing of deliveries of dichorionic diamniotic twins and complication occurred.

Total cases met the inclusion criteria. They were classified into 3 groups according to the gestational age at delivery: less than 32

weeks' gestation (group A), between 32 and 35+6 weeks' gestation (group B), and over 36 weeks' gestation (group C).

Clinical factors including maternal age, parity, and presence of premature uterine contraction, pregnancy (spontaneous or induction), presence of maternal medical history, presence of premature rupture of membrane, cervical dilatation, maternal complication, and perinatal complication were analyzed for each group.

**Results**

We reviewed 150 cases of dichorionic diamniotic twin pregnancies delivered at Elshatby University Maternity Hospital.

Among 150 Twin deliveries; 23.33% (35/150) were in group A, 36% (54/150) in group B and 40.67% (61/150) in group C.

The mean gestational age of admission was 30.8 weeks; 25.4 weeks in group A, 31.8 weeks in group B, and 35.9 weeks in group C. The mean maternal age was 24.83 years.

Preterm birth risk was relatively low for women in their late thirties. Risks for adverse outcomes were higher among younger women. (Table 1)

In our study assisted reproductive technology-conceived twin pregnancies are at greater risk than spontaneous conceived ones for pregnancy complications and adverse perinatal outcome. (Table 2) We evaluated the effect of parity and a history of preterm delivery on the outcome of twin gestation. And found that nulliparous women delivered at an earlier gestational age than multiparous women without a history of preterm delivery. (Table 2)

Twin pregnancy constitutes a high-risk factor for spontaneous early preterm delivery. The uterine contractions occurred more frequently in group A (6.5 times/30 min) and B (6.3 times/30 min) compared with in group C (2.8 times/30 min) (P<0.001). The cervical dilatation at admission in group A was statistically significant compared with the other two groups (P<0.001). PROMs (P=0.042) and incompetent internal os of cervix (IIOC, P<0.001) were represented as major clinical factors affecting for timing of delivery in twins before 36 weeks of gestation. And all IIOC had occurred before 32 weeks of gestation. However, pregnancy induced hypertension; gestational diabetes and others did not affect the timing of delivery in twins in this study. (Table 3, 4)

In our study, the incidence of FGR significantly decreased as the gestational age at delivery advanced. (Table 5)

In our study, the incidence of NICU admission was significantly higher at group A of gestation. It decreased and disappeared at higher gestational ages. And most common perinatal complication was neonatal respiratory distress syndrome which is highly presented in group A. (Table 6)

Administration of corticosteroids to stimulate fetal lung maturation has been beneficial for twin. (Table 6)

**Table (1): Comparison between the three studied groups according to age.**

	Group A (n = 35)	Group B (n = 54)	Group C (n = 61)	F	p
Age (years)					0.003*
Min. – Max.	18.0 – 35.0	16.0 – 39.0	16.0 – 40.0	5.882*	
Mean ± SD.	26.54±5.14	24.83±5.96	28.62±6.31		
Median	27.0	25.0	28.0		
Sig. bet. grps.	p1=0.382,p2=0.227,p3=0.002*				

F: F for ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)

p: p value for comparing between the three groups  
 p1: p value for comparing between group A and group B  
 p2: p value for comparing between group A and group C  
 p3: p value for comparing between group B and group C  
 \*: Statistically significant at  $p \leq 0.05$   
 Group A: Less than 32 weeks' gestation.  
 Group B: Between 32 and 35+6 weeks' gestation.  
 Group C: And over 36 weeks' gestation

**Table(2): Comparison between the three studied groups according to obstetric data.**

	Group A (n = 54)		Group B (n = 54)		Group C (n = 61)		$\chi^2$	p
	No.	%	No.	%	No.	%		
<b>Pregnancy</b>								
Spontaneous	21	60.0	31	57.4	51	83.6	10.732*	0.005*
ICSI /IUI	14	40.0	23	42.6	10	16.4		
<b>Parity</b>								
Primipara	18	51.4	26	48.1	14	23.0	10.803*	0.005*
Multiparty $\geq 1$	17	48.6	28	51.9	47	77.0		

$\chi^2$ : Chi square test  
 p: p value for comparing between the three groups  
 \*: Statistically significant at  $p \leq 0.05$

**Table(3): Comparison between the three studied groups according to C/O.**

	Group A (n = 35)		Group B (n = 54)		Group C (n = 61)		$\chi^2$	p
	No.	%	No.	%	No.	%		
<b>C/O</b>								
PTLP	30	85.7	38	70.4	6	9.8	66.166*	<0.001*
PROM	9	25.7	21	38.9	11	18.0	6.333*	0.042*
Labour pain	0	0.0	2	3.7	46	75.4	89.166*	<0.001*
IIOC**	8	22.9	0	0.0	0	0.0	20.285*	<0.001*

$\chi^2$ : Chi square test PTLP: preterm labour pain PROM: premature rupture of membranes  
 p: p value for comparing between the three groups  
 \*: Statistically significant at  $p \leq 0.05$  \*\*: incompetent internal Os of cervix

**Table(4): Comparison between the three studied groups according to medical history.**

	Group A (n = 35)		Group B (n = 54)		Group C (n = 61)		$\chi^2$	p
	No.	%	No.	%	No.	%		
<b>Medical History</b>								
No	26	74.3	28	51.9	29	47.5	6.850*	0.033*
Yes	9	25.7	26	48.1	32	52.5		
Anemic	7	20.0	16	29.6	15	24.6	1.071	0.585
Pregnancy induced hypertension	2	5.7	10	18.5	13	21.3	4.104	0.128
Gestational diabetes mellitis	0	0.0	3	5.6	0	0.0	3.747	$M_C p=0.057$
Urinary tract infection	0	0.0	1	1.9	1	1.6	0.785	$M_C p=1.000$
Bronchial asthma	0	0.0	3	5.6	3	4.9	1.746	$M_C p=0.441$
Cardiac diseases	0	0.0	0	0.0	2	3.3	1.960	$M_C p=0.335$
Hypothyroidism	0	0.0	1	1.9	1	1.6	0.785	$M_C p=1.000$

$\chi^2$ : Chi square test MC: Monte Carlo  
 p: p value for comparing between the three groups  
 \*: Statistically significant at  $p \leq 0.05$

**Table(5): Comparison between the three studied groups according to demographic data of 1stand 2nd fetus.**

	Group A (n = 35)		Group B (n = 54)		Group C (n = 61)		Test of Sig.	p
	No.	%	No.	%	No.	%		
<b>1<sup>st</sup> fetus</b>								
Gender								
Male	16	45.7	25	46.3	28	45.9	$\chi^2=0.003$	0.998
Female	19	54.3	29	53.7	33	54.1		
Presentation								
CP	23	65.7	46	85.2	58	95.1	$\chi^2=14.792^*$	0.001*
Breech	12	34.3	8	14.8	3	4.9		
TV	0	0.0	0	0.0	0	0.0		
Weight (kg)								
Min. - Max.	0.25 - 2.0		0.85 - 2.50		1.90 - 3.0			
Mean $\pm$ SD.	0.95 $\pm$ 0.34		1.94 $\pm$ 0.30		2.57 $\pm$ 0.28		F = 324.040*	<0.001*
Median	0.90		2.0		2.60			
Sig. bet. grps.	$p_1 < 0.001^*, p_2 < 0.001^*, p_3 < 0.001^*$							
<b>2<sup>nd</sup> fetus</b>								
Gender								
Male	22	62.9	27	50.0	25	41.0	$\chi^2=4.272$	0.118
Female	13	37.1	27	50.0	36	59.0		
Presentation								
CP	14	40.0	22	40.7	33	54.1	$\chi^2=3.695$	0.449
Breech	18	51.4	24	44.4	22	36.1		
TV	3	8.6	8	14.8	6	9.8		
Weight (kg)								
Min. - Max.	0.24 - 1.90		1.20 - 2.40		1.60 - 3.0			
Mean $\pm$ SD.	0.93 $\pm$ 0.33		1.86 $\pm$ 0.29		2.46 $\pm$ 0.33		F = 261.372*	<0.001*
Median	0.90		1.90		2.50			
Sig. bet. grps.	$p_1 < 0.001^*, p_2 < 0.001^*, p_3 < 0.001^*$							

$\chi^2$ : Chi square test F: F for ANOVA test, Pairwise comparison bet. each 2 groups was done using Post Hoc Test (Tukey)  
 p: p value for comparing between the three groups  
 p1: p value for comparing between group A and group B  
 p2: p value for comparing between group A and group C  
 p3: p value for comparing between group B and group C  
 \*: Statistically significant at  $p \leq 0.05$

**Table(6): Comparison between the three studied groups according to different parameters.**

	Group A (n = 35)		Group B (n = 54)		Group C (n = 61)		$\chi^2$	p
	No.	%	No.	%	No.	%		
<b>NICU</b>								
No	0	0.0	45	83.3	61	100.0	113.819*	<0.001*
Yes	35	100.0	9	16.7	0	0.0		
<b>DEXA complete course</b>								
No	34	97.1	34	64.2	44	72.1	12.802*	0.002*
Yes	1	2.9	19	35.8	17	27.9		
<b>Operation</b>								
No cerclage	27	77.1	40	74.1	51	83.6	1.614	0.446
Cerclage	8	22.9	14	25.9	10	16.4		

$\chi^2$ : Chi square test  
 p: p value for comparing between the three groups  
 \*: Statistically significant at  $p \leq 0.05$

**Discussion**

Twins are at higher risk for adverse perinatal outcomes compared to singleton gestation, predominantly due to increased risks for preterm delivery (24).

The incidence of preterm delivery and prematurity towards neonatal morbidity in twin pregnancies is significantly reduced as a result of improved neonatal care facilities (25).

Therefore, the ideal time for delivery of a pregnancy would be when the risk for perinatal morbidity and mortality is lowest.

This study has demonstrated that in twin pregnancies there is a high risk of preterm delivery that is about 85%, 70.4%, and 9.8% for birth A, B, and C group respectively. In about 80% of cases of preterm delivery, this is the consequence of spontaneous labor or PPRM, rather than medically indicated. This study confirms that the finding of a twin pregnancy constitutes a high-risk factor for spontaneous early preterm delivery. While twin pregnancy is associated with increased risk for most adverse perinatal outcomes, this analysis did not find advanced maternal age to be an additional risk factor for fetal death and infant death. Data from IVF pregnancies suggests that AMA may not be a risk factor for preterm birth with twins. (26)

GA at delivery is significantly increased in parous women carrying a multifetal gestation after controlling for other factors that affect GA at birth. (27)

Several studies have shown that pregnancies obtained by assisted reproductive technologies (ART) are associated with unfavorable obstetric and neonatal outcome such as increased incidence of pregnancy-induced hypertension (PIH), placenta previa, and preterm delivery, cesarean Section, low-birth-weight and small-for gestational-age (SGA) neonates. (28-33)

The explicit reason(s) for this less favorable outcome is largely unknown.

In the present study, we found that ART-conceived twin pregnancies are at higher risk for pregnancy complications and, consequently, are less likely to have a favorable perinatal outcome.

In conclusion, our current study suggests that ART-conceived twin pregnancies are inherently at higher risk than spontaneous conceived twin pregnancies, putting them in "double jeopardy" as a twin pregnancy and an ART-conceived one. (34-35)

In this study, clinical factors influencing the timing of delivery in twins were the frequency of uterine contraction, presence of premature rupture of membranes and dilatation of cervix. Other distributing factors for timing of delivery are Maternal age, Parity, Pregnancy (spontaneous or induction) and Maternal medical history among maternal complications were closely related to timing of delivery.

Most importantly, the frequency of uterine contraction, presence of premature rupture of membranes and dilatation of cervix are related with preterm labor. These factors should be considered treating twin pregnancies, specially at an admission and delivery.

In our study, the incidence of NICU admission was significantly higher at group A of gestation. It decreased and disappeared at higher gestational ages. The most common perinatal complication was neonatal respiratory distress syndrome which is highly presented in group (A).

In group B, we observed that using tocolytics is the important management to delay the delivery for decreasing of perinatal complications. In our series, the incidence of FGR significantly decreased as the gestational age at delivery advanced. This might be explained by the fact that complicated pregnancies with FGR might need to be terminated earlier. Moreover, the mean birth

weights increased steadily with advancement of the gestational age. Twins can continue to grow in utero till 40 weeks.

#### Conflict of interest

No potential conflict of interest relevant to this article was reported.

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#### REFERENCES

- Russell RB, Petrini JR, Damus K, Mattison DR, Schwarz RH. The changing epidemiology of multiple births in the United States. *Obstet Gynecol* 2003; 101:129-35.
- Martin JA, Park MM. Trends in twin and triplet births: 1980-97. *Natl Vital Stat Rep* 1999; 47(24):1-16.
- Hamilton B, Martin JA, Osterman MJK, Curtin SC, Mathews TJ. Births: Final Data for 2014. *Natl Vital Stat Rep* 2015; 64(12):1-64.
- Sadler TW. *Longman Medical Embryology*. 10th ed. United States: Philadelphia: Lippincott Williams & Wilkins; 2006. p.104-8.
- Barbara LH, Robyn H, Scott R. *Williams wards Obstetrics*. 24th ed. United States: New York: McGraw-Hill Education; 2014.
- Gambon HM. *Essential of obstetrics and gynecology*, 4th edition 2006: 183-185
- Zech NH, Wisser J, Natalucci G, Riegel M, Baumer A, Schinzel A. Monochorionic-diamniotic twins discordant in gender form a naturally conceived pregnancy through postzygotic sex chromosome loss in a 47,XXY zygote. *Prenat Diagn* 2008; 28(8):759-63.
- Szymusik I, Kosinska-Kaczynska K, Bomba-Opon D, Wielgos M. IVG versus spontaneous twin pregnancies—which are at higher risk of complications? *J Matern Fetal Neonatal Med* 2012; 25(12):2725-8.
- Kim JH, Park SW, Lee JJ. Birth weight reference for triples in Korea. *J Korean Med Sci* 2010; 25(6):900-4.
- Vora NL, Ruthazer R, House M, Chelmos D. Triplet ultrasound growth parameters. *Obstet Gynecol* 2006; 107(3):694-700.
- Rana S, Hacker MR, Modest AM, Salahuddin S, Lim KH, Verlohren S, et al. Circulating angiogenic factors and risk of adverse maternal and perinatal outcomes in twin pregnancies with suspected preeclampsia novelty and significance. *Hypertension* 2012; 60(2):451-8.
- Chauhan SP, Scardo JA, Hayes E, Abuhamad AZ, Berghella V. Twins: prevalence, problems, and preterm births. *Am J Obstet Gynecol* 2010; 203(4):305-15.
- Kahn B, Lumey LH, Zybert PA, Lorenz JM, Cleary-Goldman J, D'Alton ME, et al. Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice. *Obstet Gynecol* 2003; 102(4):685-92.
- Ong SS, Zamora J, Khan KS, Kilby MD. Prognosis for the co-twin following singletwin death: a systematic review. *BJOG* 2006; 113(9):992-8.
- Blickstein I, Perlman S: Single fetal death in twin gestations. *J Perinat Med* 2013; 41(1):65-9.
- Senat MV, Porcher R, Winer N, et al: Prevention of preterm delivery by 17alpha-hydroxyprogesterone caproate in asymptomatic twin pregnancies with a short cervix: a randomized controlled trial. *Am J Obstet Gynecol* 2013; 208(3):194.e1.
- Blickstein I, Perlman S: Single fetal death in twin gestations. *J Perinat Med* 2013; 41(1):65-9.
- Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2006; 3:CD004454.
- Peaceman AM, Kuo L, Feinglass J. Infant morbidity and mortality associated with vaginal delivery in twin gestations. *Am J Obstet Gynecol* 2009; 200(4):462.
- Smith GC, Fleming KM, White IR. Birth order of twins and risk of perinatal death related to delivery in England, Northern Ireland, and Wales, 1994-2003: retrospective cohort study. *BMJ* 2007; 334(7593):576.
- Bajoria R, Kingdom J. The case for routine determination of chorionicity and zygosity in multiple pregnancy. *Prenat Diagn* 1997; 17(13):1207-25.
- Kalyoncu O, Aygun C, Cetinoglu E, Kucukoduk S. Neo-natal morbidity and mortality of late-preterm babies. *J Matern Fetal Neonatal Med* 2010; 23(7):607-12.
- Xiong X, Dickey RP, Pridjian G, Buekens P. Maternal age and preterm births in singleton and twin pregnancies conceived by in vitro fertilization in the United States. *Pediatr perinat Epidemiol* 2015; 29(1):22-30.
- Misra DP, Ananth CV. Infant mortality among singletons and twins in the United States during 2 decades: effects of maternal age. *Pediatrics* 2002; 110(6):1163-8.
- Fox NS, Rebarber A, Dunham SM, Saltzman DH. Outcomes of multiple gestations with advanced maternal age. *J Matern Fetal Neonatal Med* 2009; 22(7):593-6.
- Tarter JG, Khoury A, Barton JR, Jacques DL, Sibai BM. Demographic and obstetric factors influencing pregnancy outcome in twin gestations. *Am J Obstet Gynecol* 2002; 186(5):910-2.
- Doyle P, Beral V, Maconochie N. Preterm delivery, low birth-weight and small-for-gestational-age in liveborn singleton babies resulting from in-vitro fertilization. *Hum Reprod* 1992; 7(3):425-8.
- Births in Great Britain resulting from assisted conception, 1978-87. MRC Working Party on Children Conceived by In Vitro Fertilization. *BMJ* 1990; 300(6734):1229-33.
- Multiple pregnancies. FIVNAT (French In Vitro National). *Contracept Fertil Sex* 1995; 23(7-8):494-7.
- Pregnancies and births resulting from in vitro fertilization: French national registry, analysis of data 1986 to 1990: FIVNAT (French In Vitro National). *Fertil Steril* 1995; 64(4):746-56.
- Wang JX, Clark AM, Kirby CA, Philipson G, Petrucco O, Anderson G, et al. The obstetric outcome of singleton pregnancies following in-vitro fertilization/gamete intrafallopian transfer. *Hum Reprod* 1994; 9(1):141-6.
- Tanbo T, Dale PO, Lunde O, Moe N, Abyholm T. Obstetric outcome in singleton pregnancies after assisted reproduction. *Obstet Gynecol* 1995; 86(2):188-92.
- Seoud MA, Toner JP, Kruthoff C, Muasher SJ. Outcome of twin, triplet, and quadruplet in vitro fertilization pregnancies: the Norfolk experience. *Fertil Steril* 1992; 57(4):825-34.

34. Barlow P, Lejeune B, Puissant F, Englert Y, Van Rysselberge M, Degueudre M, et al. Early pregnancy loss and obstetrical risk after in-vitro fertilization and embryo replacement. *Hum Reprod* 1988; 3(5):671-5.
35. Petersen K, Hornes PJ, Ellingsen S, Jensen F, Brocks V, Starup J, et al. Perinatal outcome after in vitro fertilization. *Acta Obstet Gynecol Scand* 1995; 74:129-31.