

Complication rates in the second and third trimester of spontaneous twin pregnancies and twin pregnancies after *in vitro* fertilization

Jerzy FLORJANSKI¹, Mariusz ZIMMER¹, Zofia BOROWIEC¹,
Michał POMORSKI¹, Henryk FILIPOWSKI²

¹ Department of Gynecology, Obstetrics and Neonatology, Wrocław Medical University, Poland

² Department of Pathophysiology, Wrocław Medical University, Poland

Correspondence to: Jerzy Florjański, MD., PhD.
Department of Gynecology Obstetrics and Neonatology,
Wrocław Medical University
Ul. Dąbrowskiego No. 5/7, 50-528 Wrocław, Poland.
TEL: +48717331400; FAX: +48717331409; E-MAIL: jerzyflorjanski@wp.pl

Submitted: 2010-01-19 Accepted: 2010-03-12 Published online: 2010-06-30

Key words: **twin pregnancy; *in vitro* fertilization; complications**

Neuroendocrinol Lett 2010; **31**(3):384–389 PMID: 20588249 NEL310310A04 © 2010 Neuroendocrinology Letters • www.nel.edu

Abstract

BACKGROUND: Most authors agree that the twin pregnancies have a higher risk of complications compared to singleton pregnancies. However, there is no unanimity as to whether the risk of complications in twin pregnancies resulting from *in vitro* fertilization is higher than in twin pregnancies resulting from spontaneous conception.

OBJECTIVE: The aim of this study was to estimate the frequency rates of complications in the second and third trimester of dichorionic-diamniotic twin pregnancies resulting from IVF (group I) compared to dichorionic-diamniotic and monochorionic-diamniotic twin pregnancies resulting from spontaneous conception (group II and III).

RESULTS: The rate of cesarean section and cervical cerclage was significantly higher in the group I. Polyhydramnios occurred less frequently in group I than in group III. The discordant growth of fetuses occurred significantly more frequently in the group I. The frequency of other complications did not differ in the studied groups. The Apgar score was similar in the group I and II but significantly lower in the group III compared to the group I.

CONCLUSIONS: 1) The frequency of complications in twin pregnancies after IVF is similar to those in the twin pregnancies conceived spontaneously. 2) In the twin pregnancies after IVF it is necessary to expect only a higher frequency of caesarean sections, cervical incompetence and a discordant growth of the twins when comparing with twin pregnancies conceived spontaneously. 3) In the twin pregnancies after IVF the intrauterine fetal demise and polyhydramnios occurred less frequently than in monochorionic-diamniotic pregnancies after spontaneous conception.

Abbreviations:

ART - assisted reproductive techniques
IVF - *in vitro* fertilization
ICSI - intracytoplasmic sperm injection
FET - frozen embryo transfer

INTRODUCTION

Within the last 15 years, the number of twin pregnancies all over the world has grown by 50–60% (Ayres & Johnson 2005; Collins 2007; Nicolaides & Węgrzyn 2006; Pison & D'Addato 2006; Ramsey & Repke 2003). In Poland, the deliveries of twin fetuses constitute approx. 1% of all the deliveries. 75% of all twin pregnancies is dizygotic and 25% monozygotic (Nicolaides & Węgrzyn 2006; Sawicki & Sawicka 2003). The most significant factors that influence the higher rates of twin pregnancies, are nowadays as follows: advanced maternal age, the changes in the environment and first of all a wider and more effective use of assisted reproductive techniques including in vitro fertilization and ovarian stimulation (Ayres & Johnson 2005; Blondel *et al.* 2006; Malinowski *et al.* 2006).

Most authors agree that the twin pregnancies have a higher risk of complications, concerning the course of pregnancy itself, as well as the morbidity and mortality of fetuses and neonates, compared to singleton pregnancies (Bornstein *et al.* 2009; Pinborg 2005; Rauh-Hein *et al.* 2009; Szymański *et al.* 2009; Buresova *et al.* 2008; Velemínský Sr. *et al.* 2008; Florjański *et al.* 2009). However, there is no unanimity as to whether the risk of complications in twin pregnancies resulting from *in vitro* fertilization is higher than in twin pregnancies resulting from spontaneous conception (Helmerhorst *et al.* 2004).

The aim of this study was to estimate the frequency rates of complications in the second and third trimester of dichorionic-diamniotic twin pregnancies resulting from IVF compared to dichorionic-diamniotic and monochorionic-diamniotic twin pregnancies resulting from spontaneous conception.

MATERIAL AND METHODS

The study included 572 twin pregnancies, delivered in the Department of Gynecology, Obstetrics and Neonatology of the Wrocław Medical University, from 1st January 1995 till 31st July 2009.

The twin pregnancies were divided into three groups. The first one consisted of 115 twin pregnancies achieved through IVF. All pregnancies in this group were dichorionic-diamniotic pregnancies, resulting from the transfer of two fresh embryos. The second group consisted of 303 dichorionic-diamniotic twin pregnancies conceived spontaneously. In the third group we surveyed 154 monochorionic-diamniotic twin pregnancies also conceived spontaneously.

Chorionicity and amnionicity were established by the use of ultrasonography in the first and second trimester of pregnancy, which is consistent with the procedures proposed by other authors (Baghdadi *et al.* 2003; Lee *et al.* 2006; Levy *et al.* 2003; Taylor 2006). The following features were taken into account: occurrence of the “lambda” or “tau” sign, the number and location

of placentas, thickness of the dividing membranes and sex of the fetuses. The pregnant women for whom the chorionicity and amnionicity could not be established were excluded from the study. As a discordant growth of the twins we assumed a difference in the birth weights higher than 15%. The difference was calculated with the following formula:

$$\frac{\text{weight of the bigger fetus} - \text{weight of the smaller fetus}}{\text{weight of the bigger fetus}} \times 100\%$$

In the I trimester the standard fetal ultrasonographic assessment was carried out (Czuba *et al.* 2007).

Clinical data of the pregnant women, complications in the course of pregnancies and the data concerning the fetuses received in group I (pregnancies after IVF), were compared to those received in group II (dichorionic-diamniotic pregnancies resulting from spontaneous conception) and group III (monochorionic-diamniotic pregnancies resulting from spontaneous conception). The chi square test was performed for the statistic analysis. As statistically significant we considered the *p*-value below 0.05.

RESULTS

The data concerning the patients from the studied groups are presented in Table 1. Table 2 presents the data concerning the pregnancy complications and the Table 3 – the assessment of the status of the neonates.

DISCUSSION

The increasing number of twin pregnancies, including pregnancies resulting from IVF, causes that their proper management has become more significant. The proper medical management of twin pregnancies resulting from IVF requires information what kind of complications and with what frequency can occur, as well as whether the frequency of occurrence of these complications differs from the twin pregnancies resulting from spontaneous conception.

So far, complications in the twin pregnancies resulting from IVF have been investigated in different aspects. Only in few publications the chorionicity and amnionicity of the twin pregnancies were taken into account. Shebl *et al.* (2009) revised the studies that compared complications in twin pregnancies achieved through assisted reproductive techniques (ART) with a group of spontaneously conceived twin pregnancies (without the division into monochorionic and dichorionic ones). These authors indicated a higher percentage of caesarean sections, preterm deliveries and low birth weight of the neonates in the group of twin pregnancies achieved through ART, compared to the twin pregnancies after spontaneous conception. They proposed that the physicians should inform their patients about a higher risk

of complications when performing a multiple embryo transfer. Similar results were presented by Manoura *et al.* (2004). These authors compared the course of the twin pregnancies and the birth status of the neonates in 73 pregnancies achieved through IVF and in 148 twin pregnancies conceived spontaneously. They indicated a higher risk of obstetric and neonatal complications in the group of twin pregnancies resulting from IVF. In this study neither the chorionicity nor amnionicity of the twin pregnancies was taken into account.

Holliday (2007) also observed a higher frequency of preterm deliveries, low birth weight of the neonates and other obstetric complications in the group of twin pregnancies achieved through IVF, compared to those resulting from spontaneous conception. Similar results were presented by Saygan-Karamursel *et al.* (2006), Verstraelen *et al.* (2005) and Bibby & Stewart (2004).

Helmerhorst *et al.* (2004) analyzed 25 publications that compared complications occurring in the singleton and twin pregnancies resulting from ART with singleton and twin pregnancies conceived spontaneously. They discovered that singleton pregnancies achieved through ART have significantly more obstetric complications than singleton pregnancies conceived spontaneously. In opposition to that, twin pregnancies after ART have significantly better perinatal outcome than twin pregnancies after natural conception.

In a cohort study Ombelet *et al.* (2005) did not indicate any statistically significant differences between twin pregnancies after intracytoplasmic sperm injection (ICSI) and those resulting from natural conception concerning the duration of pregnancy, birth weight, Apgar score, perinatal death and congenital malformations.

Suzuki *et al.* (2009) compared the frequency of complications in 64 twin pregnancies conceived by IVF with 87 twin pregnancies conceived spontaneously. They took into account only primigravidae in dichorionic-diamniotic twin pregnancies aged 35 and more. In the group conceived by IVF only the frequency of caesarean sections was higher than in the control group. The duration of the pregnancy, neonates' birth weight, Apgar score, umbilical arterial pH as well as obstetric com-

plications such as: preeclampsia, gestational diabetes, placental abruption, placenta praevia, birth weight discordance and fetal demise were similar in both groups.

Szymborska *et al.* (2007) surveyed 59 twin pregnancies after natural conception and after IVF, IVF-ICSI and FET. They did not indicate differences in the birth weight between those groups. The differences in the birth status of neonates resulted only from the duration of the pregnancy, not from the mode of conception. The authors observed a high percentage of caesarean sections (96,6%) – mainly elective ones.

Our study revealed that the age of the pregnant women was significantly higher in the group I compared to the group II and III (Table 1). We also found significantly more primigravidae in the first group. In our opinion, this results from the fact, that in Poland in vitro fertilization has not been refunded by the state, hence the necessity of gathering funds for these procedures delayed the possibility of conception (Velemínský & Tošner 2008; Velemínský Jr. *et al.* 2008a,b).

Comparing the duration of pregnancy between the investigated groups (Table 2) we did not find any significant differences. The gestational age at the delivery was approximately 35 weeks. The cesarean section rate was significantly higher in the group I compared to the group II and III. This resulted mainly from a bad obstetric history and from mothers' fear of their children, not from strictly obstetric indications. The frequency of the complications such as: gestational hypertension and preeclampsia, gestational anemia, thrombocytopaenia and HELLP syndrome, placenta praevia, previous caesarean section scar dehiscence, gestational cholestasis, urinary tract infection, premature rupture of membranes, gestational diabetes, uterine fibroids and crural varices – did not differ in the studied groups. Cervical cerclage was performed significantly more frequently in the group I than in the group II and III. It may result from the higher age of women in the group I. Polyhydramnios occurred with a similar frequency in the group I and II, and less frequently in group I than in group III.

The number of live-born neonates, their sex, average birth weight, number of congenital malformations, as

Tab. 1. The clinical data of all patients (n=572).

Clinical data	Group I (n=115) (twin pregnancies after IVF)	Group II (n=303) (dichorionic-diamniotic twin pregnancies after spontaneous conception)	p-values ^a	Group III (n=154) (monochorionic-diamniotic twin pregnancies after spontaneous conception)	p-values ^b
Age (years)	31.0±4.0	28.7±5.2	0.0001	28.1±5.3	0.0001
Primigravidae (n,%)	81 (70.4%)	112 (36.9%)	0.001	82 (53.2%)	0.001
1 st delivery (n,%)	98 (85.2%)	140 (46.2%)	0.0001	88 (57.1%)	0.0001

^a Comparison between group I and II

^b Comparison between group I and III

Tab 2. Pregnancy outcome.

	Group I (n=115) (twin pregnancies after IVF)	Group II (n=303) (dichorionic-diamniotic twin pregnancies after spontaneous conception)	p-values ^a	Group III (n=154) (monochorionic-diamniotic twin pregnancies after spontaneous conception)	p-values ^b
Duration of pregnancy (weeks)	35.4±3.1	35.6±3.8	N.S.	34.8±3.7	N.S.
< 32 weeks	15 (13.0%)	39 (12.9%)	N.S.	32 (20.8%)	N.S.
32-37 weeks	74 (64.4%)	161 (53.2%)	N.S.	83 (53.8%)	N.S.
> 37 weeks	26 (22.6%)	103 (33.9%)	N.S.	39 (25.4%)	N.S.
Caesarean section (n, %)	110 (95.6%)	198 (65.3%)	0.0001	121 (78.6%)	0.0001
Hypertension, preeclampsia (n, %)	14 (12.1%)	22 (7.2%)	N.S.	11 (7.1%)	N.S.
Anaemia (n, %)	9 (7.8%)	35 (11.5%)	N.S.	12 (7.7%)	N.S.
Thrombocytopenia and HELLP syndrom (n, %)	0 (0.0%)	2 (0.6%)	N.S.	6 (3.9%)	N.S.
Placenta praevia (n, %)	2 (1.7%)	3 (0.9%)	N.S.	1 (0.6%)	N.S.
Previous Caesarean section scar dehiscence (n, %)	0 (0.0%)	4 (1.3%)	N.S.	1 (0.6%)	N.S.
Cholestasis (n, %)	7 (6.0%)	16 (5.2%)	N.S.	11 (7.1%)	N.S.
Cervical cerclage (n, %)	23 (20.0%)	34 (11.2%)	0.03	10 (6.4%)	0.002
Urinary tract infections (n, %)	9 (7.8%)	16 (5.2%)	N.S.	4 (2.6%)	N.S.
Premature rupture of membranes (n, %)	35 (30.4%)	84 (27.7%)	N.S.	33 (21.4%)	N.S.
Polyhydramnios (n, %)	1 (0.8%)	5 (1.6%)	N.S.	11 (7.1%)	0.03
Diabetes (n, %)	1 (0.8%)	6 (1.9%)	N.S.	1 (0.6%)	N.S.
Uterine fibroids (n, %)	0 (0.0%)	4 (1.3%)	N.S.	4 (2.6%)	N.S.
Crural varices (n, %)	0 (0.0%)	3 (0.9%)	N.S.	1 (0.6%)	N.S.

N.S. – not statistically significant

^a Comparison between groups I and II^b Comparison between groups I and III

well as the number of fetuses wrapped with the umbilical cord did not significantly differ in the surveyed groups (Table 3). The discordant growth of fetuses occurred significantly more frequently in the group I than in group II and III. The occurrence of intrauterine fetal demise was similar in group I and II and significantly lower in group I compared to group III. The fetal Apgar score was also similar in the group I and II but significantly lower in the group III compared to the group I.

CONCLUSIONS

The frequency of complications in dichorionic-diamniotic twin pregnancies after IVF is similar to those in the dichorionic-diamniotic and monochorionic-diamniotic twin pregnancies conceived spontaneously.

In the twin pregnancies after IVF it is necessary to expect only a higher frequency of caesarean sections, cervical incompetence and a discordant growth of the twins when comparing with dichorionic-diamniotic and monochorionic-diamniotic twin pregnancies conceived spontaneously.

In the twin pregnancies after IVF the intrauterine fetal demise and polyhydramnios occurred less frequently than in monochorionic-diamniotic pregnancies after spontaneous conception. The birth status of neonates is also better according to the Apgar score.

REFERENCES

- 1 Ayres A, Johnson TR (2006). Management of multiple pregnancy: prenatal care-part I. *Obstet Gynecol Surv.* **60**: 527–537.
- 2 Baghdadi S, Gee H, Whittle MJ, Khan KS (2003). Twin pregnancy outcome and chorionicity. *Acta Obstet Gynecol Scand.* **82**: 18–21.
- 3 Bibby E, Stewart A (2004). The epidemiology of preterm birth. *Neuroendocrinol Lett.* **25** Suppl 1: 43–47.
- 4 Blondel B, Macfarlane A, Gissler M, Breart G, Zeitlin J (2006). Preterm birth and multiple pregnancy in European countries participating in the PERISTAT Project. *BJOG.* **113**: 528–535.
- 5 Bornstein E, Proudfit CL, Keeler SM (2009). Prematurity in twin pregnancies. *Minerva Ginecol.* **6**: 113–126.
- 6 Buresova G, Velemínský M Jr., Velemínský M Sr. (2008). Health related quality of life of children and adolescents with Type 1 diabetes. *Neuroendocrinol Lett.* **29**: 1045–1053.
- 7 Collins J (2007). Global epidemiology of multiple birth. *Reprod Biomed Online.* **15**: 45–52.

Tab. 3. Fetuses' and neonates' outcome.

	Group I (n=115) (twin pregnancies after IVF)	Group II (n=303) (dichorionic-diamniotic twin pregnancies after spontaneous conception)	p-values ^a	Group III (n=154) (monochorionic-diamniotic twin pregnancies after spontaneous conception)	p-values ^b
Live-born children (n, %)	226 (98.3%)	590 (97.4%)	N.S.	292 (94.8%)	N.S.
Male (n, %)	103 (44.8%)	282 (46.5%)	N.S.	161 (52.3%)	N.S.
Female (n, %)	127 (55.2%)	324 (53.5%)	N.S.	147 (47.7%)	N.S.
Perinatal death (n, %)	4 (1.7%)	16 (2.6%)	N.S.	16 (5.2%)	0.03
Birth weight (g) (mean ± SD)	2180.8 ± 564.5	2256.8 ± 681.1	N.S.	2061.3 ± 715.2	N.S.
Malformations (n, %)	3 (1.3%)	12 (1.9%)	N.S.	11 (3.6%)	N.S.
Discordant growth of fetuses (n, %)	55 (47.8%)	88 (29.0%)	0,001	46 (29.9%)	0.001
Fetus wrapped with umbilical cord (n, %)	5 (4.3%)	17 (2.8%)	N.S.	4 (1.3%)	N.S.
Apgar score of fetus I, at 1 st min. (mean ± SD)	6.9 ± 2.0	7.0 ± 2.5	N.S.	6.4 ± 2.7	0.002
Apgar score of fetus II at 1 st min. (mean ± SD)	7.8 ± 2.0	7.8 ± 2.3	N.S.	7.2 ± 2.6	0.002
Apgar score of fetus I, at 5 th min. (mean ± SD)	7.2 ± 2.0	7.2 ± 2.5	N.S.	6.5 ± 2.7	0.002
Apgar score of fetus II at 5 th min. (mean ± SD)	8.0 ± 1.9	8.0 ± 2.3	N.S.	7.1 ± 2.5	0.002

N.S. – not statistically significant; SD – standard deviation

^a Comparison between group I and II

^b Comparison between group I and III

- 8 Czuba B, Borkowski D, Cnota W, Sieroszewski P, Grettka K, Pietryga M, et al (2007). Ultrasonographic assessment of fetal nuchal translucency (NT) at 11th and 14th week of gestation-Polish multicentre study. *Neuroendocrinol Lett.* **28**: 175–181.
- 9 Florjanski J, Zimmer M, Pomorski M, Wiatrowski A (2009). Nonimmune hydrops fetalis. *Neuroendocrinol Lett.* **30**: 450–452.
- 10 Helmerhorst FM, Parquin DA, Doker D, Kriese MJ (2004). Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. *BMJ.* **328**: 261–266.
- 11 Holliday J (2007). Outcomes of IVF conceptions: are they different? *Res Clin Obstet Gynecol.* **21**: 67–81.
- 12 Lee YM, Cleary-Goldman J, Thaker HM, Simpson LL (2006). Antenatal sonographic prediction of twin chorionicity. *Am J Obstet Gynecol.* **195**: 863–867.
- 13 Levy R, Arfi JS, Mirlisse V, Jacob D (2003). Ultrasonic diagnosis of chorionicity in multiple pregnancies. *Gynecol Obstet Fertl.* **31**: 960–963.
- 14 Malinowski W, Kempia J, Bręborowicz GH (2006). Ciąża wielopłodowa. [(Multiple gestation.) (In Polish.)] In: Bręborowicz GH, editor. Ciąża wysokiego ryzyka. [(High risk pregnancy.) (In Polish.)] Poznań: Ośrodek Wydawnictw Naukowych, p. 183–206.
- 15 Manoura A, Korakaki E, Hatzidaki E, Bikouvarakis S, Papageorgiou M, Giannakopoulou C (2004). Perinatal outcome of twin pregnancies after in vitro fertilization. *Acta Obstet Gynecol Scand.* **83**: 1079–1084.
- 16 Nicolaidis KH, Węgrzyn P (2006). Multiple pregnancy at 11+0 – 13+6 weeks. *Ginek Pol* **77**: 175–183.
- 17 Ombelet W, Peeraer K, De Sutter P, Gerris J, Bosmans E, Martens G, et al (2005). Perinatal outcome of ICSI pregnancies compared with a matched group of natural conception pregnancies in Flanders (Belgium): a cohort study. *Reprod Biomed Online.* **11**: 244–253.
- 18 Pinborg A (2005). IVF/ICSI twin pregnancies: risk and prevention. *Hum Reprod Update.* **6**: 575–593.
- 19 Pison G, D'Addato AV (2006). Frequency of twin births in developed countries. *Twin Res Hum Genet.* **9**: 250–259.
- 20 Ramsey PS, Repke JT (2003). Intrapartum management of multifetal pregnancies. *Semin Perinatol.* **27**: 54–72.
- 21 Rauh-Hein JA, Rana S, Tamirez H, Wang A, Cohen B, Cohen A, et al (2009). Risk for developing gestational diabetes in women with twin pregnancies. *J Matern Fetal Neonatal Med.* **22**: 293–299.
- 22 Saygan-Karamursel B, Teksam O, Akusu T, Yurdakok M, Onderoglu L (2006). Perinatal outcomes of spontaneous twins compared with twins conceived through intracytoplasmic sperm injection. *J Perinat Med.* **34**: 132–138.
- 23 Sawicki K, Sawicka E (2003). Porody z ciąż wielopłodowych w Polsce w latach 1981–2001 według danych Głównego Urzędu Statystycznego. [(Multiple gestation deliveries in Poland in the years 1981–2001 according to the data of Main Statistical Department.) (In Polish.)] In: Bręborowicz GH, Malinowski W, Ronin-Walknowska E, editors. Ciąża wielopłodowa. [(Multiple gestation.) (In Polish.)] Poznań: Ośrodek Wydawnictw Naukowych, p. 21–25.
- 24 Shebl O, Ebner T, Sir A, Sommergruber M, Tews G (2009). The role of mode of conception in the outcome of twin pregnancies. *Minerva Ginecol.* **61**: 141–152.
- 25 Suzuki S, Miyake H (2009). Perinatal outcome of elderly primiparous dichorionic twin pregnancies conceived by in vitro fertilization compared with those conceived spontaneously. *Arch Gynecol Obstet.* **4**: 19.
- 26 Szymański S, Malinowski W, Ronin-Walknowska E (2009). Birth status and twin birth weight discordance. *Ginek Pol.* **80**: 664–669.

- 27 Szymborska T, Kamiński K, Niemiec KT, Jakimiuk AJ (2007). Perinatal outcome analysis of twin pregnancies at the Department of Obstetrics and Gynecology Central Clinical Hospital of Ministry of Interior and Administration in Warsaw in the years 2005–2006. *Folia Histochem Cytobiol.* **45**: 149–151.
- 28 Taylor MJK (2006). The management of multiple pregnancy. *Early Hum Develop.* **82**: 365–370.
- 29 Velemínský M Sr, Noll P, Hanzl M, Velemínský M Jr. (2008). Necrotizing enterocolitis in children with low birth-weight induced with mucormycose strain. *Neuroendocrinol Lett.* **29**: 1021–1025.
- 30 Velemínský M Jr, Prádná J, Velemínský M Sr, Tosner J (2008a). Relationship of amniotic-type placenta inflammation to pPROM, PROM and risk of early onset neonatal sepsis. *Neuroendocrinol Lett.* **29**: 447–450.
- 31 Velemínský M Jr, Stránský P, Velemínský M Sr, Tosner J (2008b). Relationship of IL-6, IL-8, TNF and sICAM-1 levels to PROM, pPROM, and the risk of early-onset neonatal sepsis. *Neuroendocrinol Lett.* **29**: 303–311.
- 32 Velemínský M, Tosner J (2008). Relationship of vaginal microflora to PROM, pPROM and the risk of early-onset neonatal sepsis. *Neuroendocrinol Lett.* **29**: 205–221.
- 33 Verstraelen H, Goetgeluk S, Derom C, Vansteelandt S, Derom R, Goethebeur E, et al (2005). Preterm birth in twins after subfertility treatment: population based cohort study. *BMJ.* **19**: 331–337.