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Influence of chorionicity on healthy twin pregnancy outcome

Uticaj horioniciteta na ishod zdrave blizanačke trudnoće

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Abstract

Background/Aim. It is still under debate in what sense and extent can chorionicity impact the pregnancy outcome of twins without gestational complications specific for monochorionicity. The study aimed to evaluate the effect of chorionicity on healthy twin pregnancy outcome. **Methods.** The study included patients with uncomplicated twin pregnancies after first trimester that were checked-up and delivered at the Clinic of Obstetrics and Gynecology, Clinical Center of Serbia, Belgrade during three years (2010–2013). Data regarding mother's age, comorbidities, parity, presence and type of gestational complications, chorionicity, mode and time of pregnancy ending, birth-weight and Apgar score of twins were determined. Obtained data were compared and statistically analyzed. **Results.** The study included 361 women with mean age of 33 years. Regardless of chorionicity, twins were mostly born during the 36th gestational week and received Apgar score ≥ 8. Only three monochorionic twins were stillborn, two preterm (29 and 32 gestational week) and one in term (35 gestational week) delivery. Contrary, no intrauterine fetal deaths were recorded. Monochorionicity negatively correlated with having live-born twins (OR = 0.023; CI = [0.001–0.609]; p = 0.024), but was not associated with twins condition at birth, i.e. Apgar score (p = 0.345), pregnancy ending time (p = 0.578) or any other twins characteristic. However, premature preterm membrane rupture and earlier gestational week of pregnancy ending were important confounding factors for relationship between chorionicity and pregnancy outcome. **Conclusion.** Monochorionicity increases risk for adverse pregnancy outcomes even for uncomplicated, healthy twin pregnancy, but has no influence on the condition of twins who survive until term. If appropriate surveillance and therapy are applied, both healthy twins can be delivered at term regardless of chorionicity.

Key words:
chorion; pregnancy, twin; pregnancy outcome.

Apstrakt

Uvod/Cilj. Još uvek se raspravlja u kom smislu i do kog stepena horionicitet može uticati na ishod blizanačke trudnoće bez gestacijskih komplikacija specifičnih za monohorionicitet. Studija je imala za cilj da se proceni efekat horioniciteta na ishod zdrave blizanačke trudnoće. **Metode.** Studijom su bile obuhvaćene sve trudnice sa nekomplikovanom blizanačkom trudnoćom nakon prvog trimestra koje su kontrolisane i porođene na Klinici za ginekologiju i akušerstvo Kliničkog centra Srbije u Beogradu tokom tri godine (2010–2013). Utvrđeni su podaci o starosti majke, komorbiditetima, paritetu, prisutnosti i tipu gestacijskih komplikacija, horionicitetu, načinu i vremenu završetka trudnoće, težini na rođenju i Apgar skoru blizanaca. Dobijeni podaci su upoređeni i statistički analizirani. **Rezultati.** Studijom je bila obuhvaćena 361 žena prosečne starosti od 33 godine. Bez obzira na horionicitet, blizanci su uglavnom bili rođeni tokom 36. gestacijske nedelje i dobili Apgar skor ≥ 8. Samo tri monohorionska blizanca su bila mrtvorođena, dva pre termina (29. i 32. nedelja gestacije) i jedan u terminu (35. nedelja gestacije). Nasuprot tome, nisu registrovane intrauterusne smrti plodova. Monohorionicitet je negativno korelisao sa živorođenošću blizanaca (OR = 0,023; CI = [0,001–0,609], p = 0,024) i nije bio povezan sa stanjem blizanaca na rođenju, tj. Apgar skorom (p = 0,345), vremenom završetka trudnoće (p = 0.578) ili bilo kojom drugom karakteristikom blizanaca Međutim, prevremena ruptura vodenjaka i ranije gestacijske nedelje završetka trudnoće su važni "konfaunding" faktori koji su uticali na odnos između horioniciteta i ishoda trudnoće. **Zaključak.** Monohorionicitet povećava rizik od loših ishoda trudnoće čak i kod nekomplikovane, zdrave blizanačke trudnoće, ali nema uticaj na stanje blizanaca koji prežive do termina. Uz primenu odgovarajućeg nadzora i terapije, oba zdrava blizanca mogu biti porođena u terminu bez obzira na horionicitet.

Ključne reči:
horion; trudnoća, blizanačka; trudnoća, ishod.

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Introduction

Careful monitoring and management of twin pregnancy is the basis of modern perinatology because multiple pregnancies carry an increased risk of perinatal morbidity and mortality compared with singleton pregnancies. This risk arises as a result of complications such as high incidence of preterm birth, fetal growth restriction, preeclampsia, etc. [1]. Twin pregnancies are classified according to either zygosity or chorionicity, and chorionicity rather than zygosity determines the outcome. Twin pregnancies can be divided into monochorionic (MC) or dichorionic (DC) according to placentation, and MC twins are classified as monoamniotic or diamniotic ones [2]. Apart from usual pregnancy complications, monochorionic twins develop unique type-specific perinatal complications, more often twin-twin transfusion syndrome. Consequently, it is well determined by numerous studies that monochorionicity poses the highest risk for both morbidity and mortality of twins [3]. However, it is still under debate in what sense and extent can chorionicity impact the pregnancy outcome of uncomplicated healthy twin pregnancy. Therefore, increased detailed antenatal fetal surveillance with precise first-trimester diagnostics of chorionicity is suggested for twins [4]. Determining chorionicity at early pregnancy can help obstetricians to plan the care of these patients in managing twin pregnancies and in counseling according to the local perinatal outcome [5].

The study aim was to evaluate the effect of chorionicity on outcome of uncomplicated healthy twin pregnancy.

Methods

The study prospectively included all patients with twin pregnancies who were checked-up and delivered at the Clinic of Gynecology and Obstetrics, Clinical Center of Serbia, Belgrade in three years period (2010–2013). The study was approved by the Clinic's Ethical Board and all women signed informed consent to participate in the study. After ultrasonographic confirmation of twin pregnancy and determination of chorionicity (single placental masses with T sign – monochroionicity vs. separate placentas and lambda sign – dichorionicity), women were closely monitored throughout pregnancy. Exclusion criteria for this study were first trimester miscarriage, development of twin-to-twin transfusion syndrome (TTTS), fetal growth restriction, placental pathologies and other complications specific for monochorionicity.

On the initial examination, detailed history regarding age, number of previous pregnancies and chronic illnesses (cardiovascular, endocrinologic, etc.) were taken from each patient. If patients had chronic illnesses that were not adequately treated, they were excluded from the study.

Obstetrical complications (presence and type) were registered throughout pregnancy such as presence of hypertension in pregnancy (HTA), gestational diabetes mellitus (GDM), placental problems (placental abruption, retro placental hematomas, placental insufficiency detected by small diameter and higher than expected grade of placenta on ultrasound and by pathological Doppler measures of placental vascularization), fetal growth restriction (IUGR) (fetal weight at delivery below the 10th percentile for gestational age), TTTS (presence of placental blood vessels anastomoses), perinatal asphyxia (assessed by cardiotocographic findings), other and combined comorbidities. In case of complications development, patients were excluded from the study.

Twins delivery was either vaginal or urgent or elective Caesarean Section (CS). The time of membranes rupture was noted and classified as during delivery or premature (PPROM) while the characteristics of amniotic fluid were expressed as clear or meconial. According to the gestational week in which pregnancy ended (miscarriage/ delivery), twins were considered as term or prematurely born (before 36th week of gestation). After birth, sex (male or female), weight and Apgar score of both twins were determined. We also noted if both twins were live-born or if one or both twins were stillborn. Moreover, all cases of intrauterine fetal death (IUFD) of one or both twins were registered.

Finally, as the primary outcome of this study we assessed the survival of twins throughout the whole pregnancy. Therefore, if both twins were live-born, pregnancy outcome was good while as adverse outcome we regarded IUFD or stillbirth of one or both twins. Moreover, the condition at birth of twins was assessed through their Apgar scores and if both twins had Apgar scores ≥ 8, their condition was regarded as good.

For statistical analysis, methods of descriptive (frequencies, mean value, standard deviation) and analytical (Spearman's correlation, Kruscal Wallis χ^2-test, logistic regression) statistics were applied. All assessed data were correlated with chorionicity and pregnancy outcomes. Binary logistic regression was used to construct models of relationship between pregnancy outcome and chorionicity.

Statistical significance was defined as $p < 0.05$. The SPSS ver. 15.0, Chicago IL, USA software was used for analysis.

Results

Initially study included 435 women with twin pregnancies who had 17 to 46 years of age at the time of birth [mean ± standard deviation (SD) = 33.18 ± 6.61 years]. Patients were mostly primiparous. Majority of women had no chronic illnesses, while women who reported comorbidities were regularly checked-up and on adequate therapy (Table 1). In our sample there were significantly more dichorionic twins (Table 2).

During examined pregnancy we registered hypertension in 51, diabetes in 24, placental pathologies in 8, TTTS in 8, IUGR in 15, malformations in 4, asphyxia in 13, chorioamnionits in 17 and other complications altogether in 43 cases. All of these gestational complications were more frequent in monochorionic than dichorionic twins ($p = 0.001$). According to the study criteria, due to complications we excluded 74 women from the study, while remaining 361 cases underwent further analysis.

Table 1

Frequency of assessed parameters of examined women

Parameters and their categories	Overall sample n (%)	Overall sample *p* between categories	Dichorionic (n)	Monochorionic (n)
Mothers parity				
1	278 (77)	< 0.001	262	16
2	61 (17)		56	5
3 and more	22 (6)		21	1
Mothers comorbidities				
no chronic illnesses	213 (59)	0.039	203	10
yes, but on therapy	148 (41)		136	12

Table 2

Frequency of assessed parameters of twins

Parameters and their categories	Overall sample n (%)		Overall sample *p* between categories	Dichorionic (n)	Monochorionic (n)
Chorionicity					
dichorionic	339	93.9	< 0.001	339	/
monochorionic	22	6.1		/	22
Delivery mode					
vaginal	145	40.2	< 0.001	139	6
CS planed	137	38.0		128	9
CS urgent	79	21.9		72	7
PPROM					
no	270	74.8	< 0.001	257	13
yes	91	25.2		82	9
Amniotic fluid					
clear	339	93.9	< 0.001	317	22
meconial	22	6.1		22	0
Sex twin I					
male	186	51.5	0.563	176	10
female	175	48.5		163	12
Sex twin II					
male	175	48.5	0.563	165	10
female	186	51.5		174	12
Apgar score (twin I)					
< 8	148	41.0	0.001	141	7
≥ 8	213	59.0		198	15
Apgar score (twin II)					
< 8	160	44.3	0.031	152	8
≥ 8	201	55.7		187	14
Both twins condition					
bad	183	50.7	0.792	174	9
good	178	49.3		165	13
Pregnancy outcome					
stillborn/IUFD	3	0.8	<0.001	0	3
both alive	358	99.2		339	19
Pregnancy ending time					
preterm	135	37.4	< 0.001	128	7
in term	226	62.6		211	15

PPROM – premature preterm rupture of membranes; CS – Caesarean Section; IUFD – intrauterine fetal death.

Examined healthy twins were mostly delivered by CS, usually elective. Regardless of chorionicity, twins were in average born during the 36th gestational week (range = 27 to 40; mean ± SD overall = 35.68 ± 2.56; MC = 35.81 ± 1.95; DC = 35.67 ± 2.59 gestational weeks). Only few twins (n = 27) were delivered before the 30th gestational week, all dichorionic. Moreover, significantly more twins were born in term (≥ 36th gestational week). Preterm membrane rupture

occurred in 25% of the cases, but the amniotic fluid usually had appropriate characteristics (Table 2).

In our sample of healthy twins without gestational complications only three twins were stillborn and all of them were from monochorionic pregnancies. These adverse outcomes occurred in two cases preterm (29th and 32nd GW) and in one case in term (35th GW) delivery. Contrary, no IUFDs were recorded. First twins had the mean birth weight 2,298.16 ± 621.48 grams and the mean Apgar score was 7.32 ± 1.85 (MC = 7.86 ± 0.99; DC = 7.28 ± 1.88). Second twins had the mean birth weight 2,237.53 ± 651.49 grams and the mean Apgar score was 7.28 ± 1.86 (M = 7.86 ± 0.99; DC = 7.24 ± 1.91). Nevertheless, majority of twins both monochorionic and dichorionic ones, were in good condition at birth and 59% of the first and 55.7% of the second twins received Apgar score ≥ 8 (Table 2). Therefore, the overall outcome of investigated twin pregnancies was good.

Chorionicity was correlated negatively with pregnancy outcome and positively with delivery mode (Table 3). Dichorionic twins had better survival rates. Monochorionic twins were at higher risk for adverse perinatal outcome [odds ratio (OR) = 0.023; 95% confidence interval (CI) = 0.001–0.609] and had a higher chance to be delivered by Cesarean Section (OR = 1.88; 95% CI = 1.05–3.38). Pregnancy outcome was associated with amniotic fluid characteristics, delivery time and twin birthweight, but not chorionicity. Moreover, there were no significant differences in mothers and twins characteristics or other assessed parameters regarding chorionicity.

Table 3

Correlations and differences of assessed parameters and chorionicity

Parameters		Chorionicity	Pregnancy outcome		Chorionicity
Mothers age	ρ	-0.036	0.049	χ^2	0.463
	p	0.497	0.351	*p*	0.496
Mothers parity	ρ	0.021	0.054	χ^2	0.164
	p	0.686	0.310	*p*	0.685
Chronic illnesses of the mother	ρ	0.088	-0.012	χ^2	2.785
	p	0.095	0.819	*p*	0.095
PPROM	ρ	0.092	-0.075	χ^2	3.055
	p	0.080	0.156	*p*	0.080
Amniotic fluid characteristics	ρ	-0.065	**-0.112**	χ^2	1.516
	p	0.219	**0.033**	*p*	0.218
Delivery mode	ρ	**0.776**	-0.002	χ^2	**6.266**
	p	**0.039**	0.964	*p*	**0.042**
Sex twin I	ρ	0.031	-0.025	χ^2	0.345
	p	0.558	0.631	*p*	0.557
Weight twin I	ρ	0.013	**0.401**	χ^2	0.061
	p	0.805	**0.001**	*p*	0.805
Apgar score twin I	ρ	0.042	**0.785**	χ^2	0.634
	p	0.427	**0.000**	*p*	0.426
Sex twin II	ρ	0.015	0.048	χ^2	0.085
	p	0.771	0.368	*p*	0.770
Weight twin II	ρ	0.025	**0.395**	χ^2	0.231
	p	0.631	**0.001**	*p*	0.631
Apgar score twin II	ρ	0.050	**0.837**	χ^2	0.902
	p	0.343	**0.001**	*p*	0.342
GW of delivery	ρ	-0.012	**0.316**	χ^2	0.052
	p	0.819	**0.001**	p	0.819
Pregnancy ending time (pre/in term)	ρ	0.029	**0.350**	χ^2	0.310
	p	0.578	**0.001**	p	0.577
Twins condition at birth	ρ	0.050	**0.624**	χ^2	0.895
	p	0.345	**0.001**	*p*	0.344
Pregnancy outcome	ρ	**-0.831**	/	χ^2	**7.369**
	p	**0.026**	/	*p*	**0.018**

***Note*: Significant differences are bolded.**
PPROM – premature preterm rupture of membranes; GW – gestational week; ρ – coefficient of correlation.

A significant binary logistic regression equation of relationship between pregnancy outcome and chorionicity was obtained ($\chi^2 = 5.343$; $p = 0.021$; B = 3.750; Wald = 137.356; Exp(B) = 42.5; R^2 Nagelkerke = 0.851; total classification % = 80). Model was adjusted for PPROM, delivery time and mode as well as mother's age, previous parity and illnesses: Twin pregnancy outcome = – 0.792 + 0.038 × PPROM – 0.012 × gestational week of delivery – 0.084 × chorionicity

From the obtained equation it could be seen twin pregnancy outcome was significantly associated with chorionicity. Still, occurrence of PPROM and earlier gestational week of delivery were important confounding factors that could influence the relationship between chorionicity and pregnancy outcome. Therefore, prevention of gestational complications and preterm birth are crucial to minimize the potential negative impact of monochorionicity on twins' survival and condition.

Discussion

According to the results of our study chorionicity can influence survival of otherwise healthy twins placing MC twins at greater risk. However, chorionicity does not significantly impact the condition at birth of live-born twins as well as growth and development of twins who endure up to term.

Most literature data show that monochorionic twins have higher rate of very preterm birth (before 33rd gestational week), very low birth weight (birth weight < 1,500 g), the first minute Apgar < 7 and hospitalization [1, 4]. Perinatal mortality is usually also significantly higher as well as intrauterine fetal death [6]. The prospective risk of IUFD is much higher for MC twins at all gestational ages but the highest risk is before 24–28 gestational weeks [7]. Monochorionic pregnancies carry an increased risk of both a single fetal demise and a double twin demise mostly occurring before the third trimester [8]. MC twins were also two times more likely to be stillborn than DC twins. However, the prospective risks of stillbirth is found to be low for both MC and DC twins after 32 weeks of gestation and decreases even more at higher gestational weeks especially for MC twins [9, 10]. If both fetuses are alive at 24–28 weeks, the chance of their survival until term is similar in MC and DC pregnancies [2]. Some studies have shown that mortality of MC and DC twins did not differ in deliveries after 30 weeks of gestation, probably due to the fact that modern obstetrics is more effective in reducing mortality in both MC and DC twins [1, 11]. Still, after 38 gestational weeks MC twins have a higher risk for perinatal mortality compared to DC twins. Placental vascular malperfusion is the usually the main complication of dichorionic while IUGR, placental vascular abnormalities and TTTS, abnormal cord insertion and adverse neonatal outcomes are more common in monochorionic twins [12]. In our study, no IUFDs were registered in uncomplicated healthy twin pregnancies regardless of their chorionicity. On the other hand, adverse perinatal outcomes occurred only in case of monochorionicity. All adverse outcomes happened during or close to delivery implying an additional risk for monochorionic twins that might be caused by issues of the cord (entanglement in case of single amniotic sac, etc.) or some still unknown processes that needs further investigation. However, it should be mentioned that the rate of adverse outcomes was very low and that majority of investigated twins were live-born and in good condition with high Apgar scores.

The optimal time for delivery of monochorionic twins to prevent cord entanglement, growth discrepancies and intrauterine fetal death is still controversial [13]. MC twins are mostly delivered preterm [4]. As the highest morbidity for monochorionic twins is registered in 35th and 36th GW some authors support delivery of uncomplicated monochorionic twins at completed 34 gestational weeks [14, 15]. Conversely, others think that, with a strategy of close fetal surveillance, both monochorionic and dichorionic pregnancies can be continued to ninth lunar month (36–37 gestational weeks) with minimal perinatal morbidity [16, 17]. Studies have shown that median gestational age is mostly one week longer in DC twins than in MC ones. In uncomplicated dichorionic twin pregnancies delivery should happen at 37 weeks of gestation and in monochorionic ones at 36 weeks [16, 18]. Although delivery closer to term was associated with better pregnancy outcome, chorionicity did not have any significant influence on time of delivery in our study. Investigated twins were successfully delivered mostly in the 36th gestational week regardless of their chorionicity. Consequently, it can be said that if there are no gestational complications that might indicate induction of preterm delivery, both MC and DC healthy twins should not be delivered before ninth month of gestation.

Some studies indicate that there is usually no difference in the delivery mode of twins as a function of chorionicity and consequently intrapartum management should not vary due to chorionicity [19]. Twins we followed were generally more often delivered by CS. However, MC twins had a higher chance to be delivered by CS than DC twins. On the other hand, delivery mode did not influence pregnancy outcome, so the optimal delivery mode of twins should be more thoroughly investigated in further studies.

Most literature data show that mean birth weight in DC twins is usually significantly higher than in MC ones and that MC twins are almost two times more likely to have fetal growth restriction or severe birth weight discordance (> 20%) [4, 16]. Still, other studies show that severe birth weight discordance occurs equally in twins regardless of their chorionicity [1]. There were no significant differences of birth weight between MC and DC twins in our sample.

In studies using multivariate analysis, lower gestational age at delivery, monochorionicity and growth restriction were independent predictors of adverse neonatal outcome [12]. The model we constructed showed that chorionicity did not impact pregnancy outcome even in healthy uncomplicated pregnancies. However, more attentions should be paid to prevention of PPROM and preterm birth as these two parameters were found to be significant confounding risk factors of adverse pregnancy outcome.

Conclusion

Monochorionic twins, even if healthy and uncomplicated, are at high risk for perinatal mortality. Nevertheless,

chorionicity does not significantly impact the condition at birth, growth and development of twins who manage to survive nine lunar months. Therefore, it can be said that if appropriate prenatal and peripartum surveillance and adequate therapy are applied, both healthy twins can be delivered even in term regardless of their chorionicity.

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