VIA MEDICA

ORIGINAL PAPER / OBSTETRICS

Ginekologia Polska
2016, vol. 87, no. 11, 755–762

ISSN 0017–0011

DOI: 10.5603/GP.2016.0083

Effect of morphological and functional changes in the secundines on biometric parameters of newborns from dichorionic twin pregnancies

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ABSTRACT

Objectives: The aim of the study was to determine if, and to what extent, structural and functional changes of the secundines influence biometric parameters of neonates from dichorionic twin pregnancies.

Material and methods: The study included neonates from dichorionic, diamniotic twin pregnancies, along with their secundines. Based on histopathological examination of the secundines, the mass and dimensions of the placenta, length and condition of the umbilical cord, chorionicity, focal lesions, and microscopic placental abnormalities were determined for 445 pairs of twins. Morphological development of examined twins was characterized on the basis of their six somatic traits, while birth status of the newborns was assessed based on their Apgar scores. Statistical analysis included Student t-tests, Snedecor's F-tests, post-hoc tests, non-parametric chi-squared Pearson's tests, and determination of Spearman coefficients of rank correlation.

Results: The lowest values of analyzed somatic traits were observed in twins who had placentas with velamentous or marginal cord insertion. Inflammatory lesions in the placenta and placental abruption turned out to have the greatest impact of all analyzed abnormalities of the secundines. Inflammatory lesions in the placenta were associated with lower values of biometric parameters and a greater likelihood of preterm birth. Neonates with a history of placental abruption were characterized by significantly lower birth weight and smaller chest circumference.

Conclusions: Morphological changes in the secundines have a limited impact on biometric parameters of neonates from dichorionic twin pregnancies. In turn, functional changes exert a significant effect and more often contribute to impaired fetal development.

Key words: velamentous cord insertion, marginal cord insertion, limited maternofetal exchange, inflammatory lesions of the secundines, placental abruption

Ginekologia Polska 2016; 87, 11: 755–762

INTRODUCTION

All abnormalities of the placenta may exert a significant effect on fetal development, pregnancy and birth [1, 2]. Although the placenta is formed between 15 and 18 weeks of gestation, it undergoes structural changes throughout the whole prenatal period. Developmental malformations of the placenta in early pregnancy typically result in late miscarriage; in turn, the defects observed later in pregnancy may result in disrupted maternofetal exchange, growth restriction and a risk of fetal mortality. Most placental pathologies result from maternal systemic diseases. Some conditions, such as diabetes mellitus and arterial hypertension, may impair the function of the placenta, leading to placental insufficiency. Maternal infections (e.g. toxoplasmosis, viral hepatitis) may

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predispose to the development of necrotic foci or cysts, calcification, fibrosis, inflow of inflammatory cells, vascular lesions or swelling of the placental tissue [3]. The placenta constitutes a barrier which protects the fetus against maternal infections. However, many bacteria and viruses can penetrate the placental barrier, and therefore, it does not completely protect the fetus against an infection. Also, all types of vaginitis constitute a potential threat as they may contribute to membrane rupture and placental or fetal infection. The most commonly observed pathologies of the secundines include abnormal cord insertions, bilobate placenta and the presence of an accessory placental lobe. The latter is attached to the proper placenta through blood vessels, referred to as vasa previa, that run freely within fetal membranes. Amniorrhexis may result in rupture of vasa previa, and consequently, if not detected early enough, may endanger fetal life [4, 5].

Abnormal cord insertions, such as marginal or velamentous insertion, are markedly more common in multiple than in singleton pregnancies [6–9]. According to the literature, the presence of abnormal insertions may explain, at least in part, the higher incidence of intrauterine growth restriction among twins and higher perinatal morbidity and mortality rate of fetuses and newborns from multiple pregnancies.

The presence of placenta previa and placental abruption constitute principal risks for the outcome of pregnancy and perinatal period. These conditions are principal causes of bleeding and hemorrhage during pregnancy and labor, posing a significant threat to both pregnant women and their fetuses [10–13].

A review of the available literature suggests that all abnormalities regarding structure and location of the placenta, as well as other placental pathologies, interfere with normal functioning of this organ [2, 14, 15]. In turn, functional changes in the placenta, such as limited maternofetal exchange, abnormal placental perfusion and inflammation of the secundines may impair fetal development [16–18].

OBJECTIVE

The aim of this study was to determine if, and to what extent, structural and functional changes of the secundines influence biometric parameters of neonates from dichorionic twin pregnancies.

MATERIAL AND METHODS

The study included neonates from dichorionic, diamniotic twin pregnancies, born between 22 and 41 weeks of gestation at the Gynecological-Obstetrical Clinical Hospital, Poznan University of Medical Sciences, along with their secundines. Based on the histopathological examination of the secundines, the mass and dimensions of the placenta, its histological abnormalities, and the length and condition of the umbilical cord were determined for 445 pairs of twins. In the case of shared (fused) placenta, its characteristics (pathological changes) were ascribed to each of the two twins from the pair. Histopathological examination of the secundines, conducted at the Pathology Unit of the Gynecological-Obstetrical Hospital, included macroscopic and microscopic evaluation. Pathological lesions were classified into the following groups: limited area of maternofetal exchange, placental abruption, ascending inflammation, chorionitis, and disorders of fetal or maternal circulation. The list of factors contributing to a reduced area of maternofetal exchange included diffuse lesions, such as deposition of fibrin in intervillous spaces, fibrosis, microinfarcts and necrosis, as well as focal lesions: infarcts, hemorrhages, deposits of fibrin in basal and villous layer (except for intervillous spaces), cysts, angiomas and thrombi on the maternal surface of the placenta (classified as placental abruption).

Morphological development of the twins was characterized on the basis of their somatic traits: birth weight, total body length, crown-rump length, shoulder width, head circumference, and chest circumference.

Birth status of the newborns was assessed on the basis of their Apgar scores derived from five basic clinical parameters determined at 1 and 5 min.

The neonates were grouped according to the morphological changes of the secundines, factors reducing maternofetal exchange, disorders of placental perfusion, inflammation of the secundines, and placental abruption. The following five groups of twins were identified based on the structure of the secundines:

- group 0 — newborns from pregnancies with bilobate placenta or accessory placental lobe,
- group 1 — newborns from pregnancies with marginal cord insertion,
- group 2 —newborns from pregnancies with umbilical cord pathologies, i.e. false or true knots and umbilical cord collisions,
- group 3 — newborns from pregnancies with velamentous cord insertion,
- group 4 — newborns from pregnancies with a normal placenta.

Based on the presence of factors limiting maternofetal exchange of the blood, the twins were classified into the following four groups:

- 0 — twins from pregnancies without limitations in maternofetal exchange,
- F — twins from pregnancies with large focal deposits of fibrinogen in the placenta,
- F Z — twins from pregnancies with fibrinogen deposits in the placenta and evidence of infarcts within the placental lobes,
- Z — twins from pregnancies with placental infarcts.

Analysis of variance with the F-test was used to verify the significance of intergroup differences in the values of somatic traits; post-hoc analysis was conducted with the least significant difference (LSD) test. The significance and power of relationships between pairs of variables were analyzed based on the results of Pearson's chi^2 tests and values of Spearman's rank correlation coefficients.

RESULTS

Patho-morphological changes in the umbilical cords referred both to their length and type of insertion (Table 1). The presence of a short umbilical cord (< 35 cm) was frequently associated with placental abruption, whereas a longer cord (> 100 cm) typically contributed to umbilical cord collisions and the formation of false or true knots. The most commonly observed types of cord insertion were paracentral and central types. The presence of marginal insertion was associated with pathologies of umbilical vessels, kidney or cardiac defects and an abnormal volume of amniotic fluid. Velamentous insertion, i.e. the cord inserted into the fetal membranes and traveling within them to the placenta, was the least frequently observed type of cord insertion in our series.

To examine the effect of patho-morphological changes in the secundines on somatic development of the neonates, we compared mean normalized values of analyzed traits (birth weight, total body length, crown-rump length, head and chest circumferences) in five groups of newborns identified on the basis of their placental structure (Table 2). Normalized values of analyzed somatic traits were highest in neonates with normal placentas and lowest in neonates with velamentous or marginal cord insertion (Table 2). Structural abnormalities of the secundines exerted statistically significant effects on birth weight ($p \leq 0.01$), total body length ($p \leq 0.05$) and head circumference ($p \leq 0.01$) (Table 2). Post-hoc analysis with the LSD test demonstrated that twins who had placentas with velamentous or marginal cord insertion differed from the remaining newborns in terms of birth weight ($p \leq 0.01$) and total body length ($p \leq 0.05$). Moreover, we found significant differences in head circumference of

Table 1. Distribution of the secundines [%] according to the type of umbilical cord insertion and its length [cm]

Umbilical cord length			Cord insertion				
< 35	< 35–100 >	> 100	Paracentral	Central	Marginal	Velamentous	Unspecified
46%	50%	4%	58.4%	21.2%	3.6%	1.6%	15.2%

Table 2. Descriptive statistics (N, $\bar{x}$, SD) for normalized values of somatic traits (1–5), stratified according to the morphology of the secundines (0–4), and influence of placental abnormalities on analyzed somatic parameters

Somatic traits		Morphological type of the secundines (0–4)				
		0	1	2	3	4
	N	59	32	126	7	431
Trait 1	$\bar{x}$	.319	–.449	.125	–.899	.340
	SD	.478	.457	.702	1.648	.426
	p	.000**				
Trait 2	$\bar{x}$	.229	–.917	.534	–.034	.663
	SD	.762	.673	.646	1.165	.516
	p	.013*				
Trait 3	$\bar{x}$	–.154	–.607	.078	–.685	–.029
	SD	.766	.758	.874	.903	.770
	p	.211				
Trait 4	$\bar{x}$	.486	–.191	.490	.106	.715
	SD	.343	.389	.543	.689	.447
	p	.021*				
Trait 5	$\bar{x}$	.198	–.684	.579	.011	.570
	SD	.308	.434	.876	.586	.706
	p	.055				

Traits: 1 —birth weight, 2 — total body length, 3 — crown-rump length, 4 — head circumference, 5 — chest circumference. Morphological types of the secundines (0–4) as described in the text

p — probability of statistical error; *significantly different at $p \leq 0.05$; **significantly different at $p \leq 0.01$

twins with normal placentas and those whose placentas had velamentous cord insertion (Tables 3 and 4).

Newborns with velamentous or marginal cord insertion were characterized not only by significantly lower values of nearly all analyzed somatic traits, but also presented with lower Apgar scores. Their mean Apgar scores at 1 and 5 min were the lowest of all study subgroups (Table 5). However, analysis of variance did not demonstrate statistical significance of these intergroup differences (Table 5).

Aside from the effects of structural abnormalities in the secundines on neonatal status at birth, we also studied the impact of functional changes within the placenta. Up to 71% of placentas included in our series had a limited area of maternofetal exchange. Up to 55% of the placentas had fibrinogen deposits, and slightly less than 30% showed the presence of infarcts; calcification and necrosis were markedly less frequent, occurring in 5% and 4% of the secundines, respectively. To verify which of the factors limiting maternofetal exchange exerted a significant effect on the somatic development, we compared somatic parameters for various subsets of twins (Table 6). The highest values of somatic traits were found in twins whose placentas provided normal maternofetal exchange, and the lowest in those with massive infarcts within the placenta. However, the only somatic trait that turned out to be significantly modulated by the area of maternofetal exchange was head circumference (Table 6). Post-hoc analysis with the LSD test demonstrated significant differences in the head circumfer-

Table 3. Relationship between birth weight or total body length and morphological abnormalities of the secundines — results of post-hoc analysis with the LSD test

			Birth weight				
			Type of placental structure				
			0	1	2	3	4
Total body length	Type of placental structure	0		.28337	.30581	.00013**	.91539
		1	.10283		.41646	.54551	.26630
		2	.10201	.03735*		.00049**	.19322
		3	.37942	.22700	.04323*		.00005**
		4	.02832*	.02424*	.42425	.01599*	

*Significantly different at p ≤ 0.05; **significantly different at p ≤ 0.01

Table 4. Relationship between head circumference and morphological abnormalities of the secundines – results of post-hoc analysis with the LSD test

			Head circumference				
			Type of placental structure				
			0	1	2	3	4
Head circumference	Type of placental structure	0		.18144	.98071	.08123	.10788
		1	.18144		.17397	.57246	.07253
		2	.98071	.17397		.05890	.05556
		3	.08123	.57246	.05890		.00386**
		4	.10788	.07253	.05556	.00386**	

**Significantly different at p ≤ 0.01

Table 5. Influence of pathological changes in the secundines on general status of twins expressed by Apgar scores at 1 and 5 min

Type of placental structure	N	Apgar at 1 min			Apgar at 5 min		
		$\bar{x}$	SD	p	$\bar{x}$	SD	p
0	59	7.500	1.732	0.476	8.850	1.000	0.127
1	32	7.288	1.843		8.298	1.124	
2	126	7.839	1.946		9.214	1.159	
3	7	7.143	1.952		8.143	1.345	
4	431	8.333	2.570		9.290	1.243	

Table 6. Influence of factors limiting the area of maternofetal exchange on the normalized values of somatic traits in the studied twins

Somatic traits		Type of defect in maternofetal exchange			
		0	F	F Z	Z
		N = 258	N = 288	N = 202	N = 142
Birth weight	$\bar{x}$	0.19	0.09	0.06	–0.03
	SD	0.77	0.67	0.79	1.11
	p	0.207			
Total body length	$\bar{x}$	0.39	0.36	0.30	0.28
	SD	0.79	0.70	0.82	1.23
	p	0.677			
Crown-rump length	$\bar{x}$	–0.09	–0.14	–0,20	–0,24
	SD	0.91	0.84	0.90	1.39
	p	0.573			
Head circumference	$\bar{x}$	0.51	0.47	0.34	0.30
	SD	0.58	0.57	0.66	0.86
	p	0.013*			
Chest circumference	$\bar{x}$	0.47	0.44	0.43	0.07
	SD	0.93	0.90	1.10	0.89
	p	0.462			

p — probability of statistical error; *significantly different at $p \leq 0.05$

Table 7. Influence of inflammatory lesions in the secundines on gestational age at birth and mean Apgar scores at 1 and 5 min

Inflammatory lesions	Gestational age				Apgar score at 1 min				Apgar score at 5 min			
	N	$\bar{x}$	SD	p	$\bar{x}$	N	SD	p	$\bar{x}$	N	SD	p
absent	810	35.29	2.76	**	7.75	810	2.67	**	9.00	810	1.55	**
present	80	31.95	4.53		5.99	80	3.32		7.64	80	2.37	

**Significantly different at $p \leq 0.01$

ence of twins with uninterrupted maternofetal exchange and neonates whose placentas showed evidence of massive infarcts ($p \leq 0.01$).

We also analyzed the effects of disrupted placental perfusion on somatic development of twins, comparing mean values of somatic traits for two groups of twins, with normal and disrupted placental perfusion. Twins with normal placental perfusion (5% of the study group) were characterized by higher, albeit insignificantly higher, values of all analyzed somatic traits compared with those with impaired placental perfusion (95%).

To verify an association between the inflammation of the secundines and analyzed somatic traits, we compared the values of the latter in twins with and without the evidence of inflammatory lesions in the placenta (9% vs. 91%, respectively). Despite the observation of apparently higher values in the latter group, none of the intergroup differences turned out to be statistically significant. However, placental inflammation exerted a significant effect on general status of twins at birth, as expressed by the Apgar score ($p \leq 0.01$) (Table 7). Twins with inflammatory lesions of the placenta had lower Apgar scores at 1 and 5 min and more often were born preterm than neonates with normal secundines. Furthermore, twins from the former group had three weeks younger gestational age at birth (Table 7).

In addition, we analyzed the effect of placental abruption on somatic development. Our findings imply that placental abruption negatively affected somatic development of twins. Twins with a history of placental abruption presented with lower values of somatic traits; birth weight and chest circumference of neonates from this group differed significantly from the respective parameters of twins with normal placentas ($p \leq 0.01$) (Table 8).

To determine the cumulative effect of these placental pathologies on biometric parameters of newborns, we compared somatic parameters in five groups of twins with a different number of placental abnormalities. Group 0 included newborns with no history of placental pathologies, and groups

Table 8. Effects of placental abruption on the values of somatic traits in the studied twins (group 0 – twins with normal placentas; group 1 — twins with a history of placental abruption)

Somatic traits	Group 0			Group 1			p
	N	$\bar{x}$	SD	N	$\bar{x}$	SD	
Birth weight	726	0.14	0.73	164	–0.01	0.81	0.019**
Total body length	726	0.35	0.77	164	0.35	0.87	0.916
Crown-rump length	726	–0.15	0.88	164	–0.13	1.04	0.873
Head circumference	726	0.47	0.62	164	0.38	0.58	0.088
Chest circumference	726	0.49	0.99	164	0.21	0.86	0.001**

p — probability of statistical error; **significantly different at $p \leq 0.01$

Table 9. Relationship between the number of placental pathologies and somatic parameters of the studied twins

Somatic traits		Number of placental pathologies				
		0	1	2	3	4
		N = 21	N = 256	N = 520	N = 79	N = 14
Birth weight	$\bar{x}$	0.32	0.21	0.09	–0.10	–0.06
	SD	0.48	0.70	0.75	0.87	0.60
	P	0.017*				
Total body length	$\bar{x}$	0.23	0.38	0.36	0.22	0.18
	SD	0.76	0.79	0.76	1.00	0.76
	P	0.363				
Crown-rump length	$\bar{x}$	–0.15	–0.14	–0.14	–0.26	–0.52
	SD	0.77	0.92	0.87	1.17	1.40
	P	0.450				
Head circumference	$\bar{x}$	0.49	0.53	0.43	0.31	0.08
	SD	0.34	0.60	0.61	0.69	0.08
	P	0.080				
Chest circumference	$\bar{x}$	0.60	0.60	0.42	0.13	0.06
	SD	0.31	1.02	0.95	1.00	0.38
	P	0.003**				

0–4 — number of placental pathologies, as described in the text; p — probability of statistical error; *significantly different at $p \leq 0.05$; **significantly different at $p \leq 0.01$

1, 2, 3 and 4 neonates with one, two, three and four abnormalities, respectively. Twins without placental defects or no more than one pathology presented with higher values of somatic traits than those with multiple abnormalities of the placenta (Table 9). However, analysis of variance with the F-test revealed that the study groups differed significantly solely with regards to their birth weight and chest circumference (Table 9). Post-hoc analysis with the LSD test confirmed the presence of statistically significant differences in these parameters ($p \leq 0.01$) between twins with the largest number of placental abnormalities (group 3 and 4) and those without placental pathologies or no more than one defect (group 0 and 1).

Finally, we analyzed mortality (i.e. the number of stillbirths and deaths in the first 24 h of life) of one or both twins from pregnancies with various types of placental pathologies. The chi^2 test did not confirm a significant effect of disrupted placental perfusion and reduced area of maternofetal exchange on the mortality rates. However, we found significant associations between the mortality and inflammation of the secundines ($p \leq 0.01$) or placental abruption ($p \leq 0.05$). The values of Spearman rank correlation coefficients (R), shown in Table 10, point to presence of a linear relationship between the two types of placental pathologies and perinatal mortality.

DISCUSSION

Our study showed that structural abnormalities of the secundines do not exert a significant effect on the somatic development of twins. Twins with velamentous or marginal cord insertion, representing 1.6% and 3.6% of all examined

Table 10. Relationship between mortality and various types of placental pathologies — results of chi-squared test and Spearman rank correlation coefficients

Statistics	Placental disorders			
	Impaired perfusion	Limited area of exchange	Inflammatory lesions	Placental abruption
Pearson's chi-squared test	0.388	0.118	0.000**	0.016*
Chi-squared test with Yates's correction	0.338	0.129	0.000**	0.025*
Spearman rank correlation coefficient (R)	0.389	0.118	0.000**	0.016*

*Significant at $p \leq 0.05$, **significant at $p \leq 0.01$

newborns, respectively, were the only groups whose characteristics differed significantly from those of neonates without patho-morphological changes in the secundines. They presented with both worse general status (as shown by lower Apgar scores at 1 and 5 min) and with lower values of somatic parameters. Also Szymański et al. [9] observed that twins with abnormal cord insertions are born with lower body weight and worse general status.

According to Potter and Craig [19], marginal cord insertion results in the impairment of maternofetal exchange since placental surface used to supply the fetus is reduced. The presence of marginal cord insertion was shown to be associated with higher incidence of developmental malformations and intrauterine growth restriction [7]. Our findings are consistent with these reports, since the twins with marginal cord insertion presented with lower values of somatic parameters at birth than those with normal morphology of the secundines.

In our opinion, placental causes of impaired fetal development that have been postulated in literature [20–25], seem to be linked to dysfunction of the placenta, rather than to its morphological changes.

Available data on the developmental impact of functional changes in the placenta are inconclusive. According to many authors, most macroscopic placental lesions, such as calcifications, plaques, thrombi and cysts are clinically irrelevant [21–23].

Infectious factors may penetrate to the placenta from maternal bloodstream and cause villitis. Chorioamnionitis may be also caused by microorganisms transferred from birth canal. Villitis may also develop as a consequence of specific maternal infections, such as rubella, toxoplasmosis, listeriosis, syphilis or cytomegaly. However, these diseases contribute only to a small proportion of villitis, and the etiology of the vast majority of cases remains unknown [26].

Our study showed that the presence of inflammatory lesions in the secundines was associated with worse status of twins at birth. The study conducted by Fox [26] documented a strong association between the presence of villitis and high incidence of intrauterine growth restriction, but the exact character of this relationship is unclear. According to this author, inflammatory changes in the placental villi usually contribute to intrauterine infection. An inhibitory effect of infection on the synthesis of fetal DNA may explain why fetal growth is impaired, which eventually results in low birth weight. The placenta constitutes a markedly less effective antimicrobial barrier than generally believed; in fact, virtually all identified infectious factors can penetrate the placental barrier and cause fetal infection.

Chorioamnionitis is the principal cause of preterm delivery, especially before 35 weeks of gestation [27–29]. The exact mechanism defining how ascending infection stimulates preterm delivery is still unclear; overproduction of cytokines by activated macrophages was postulated to enhance the synthesis of prostaglandins which act as a direct trigger to initiate labor [28–31]. Perinatal consequences of ascending infection may also include low birth weight, stillbirth or intrauterine death [14, 32]. Our findings confirm that placental inflammation is associated both with a decrease in biometric parameters of the neonate and with higher incidence of preterm birth and stillbirth.

Placental abruption is considered to be a significant independent predictor of preterm birth [14, 32–35]. Ananth et al. [14] showed that placental abruption is associated with a 4- to 6-fold increase in the risk of preterm birth. Observations of many authors, according to whom placental abruption affects neonatal status at birth [2, 15], also seem to be supported by the results of our study. Twins from pregnancies complicated by placental abruption presented with significantly lower birth weight and smaller chest circumference.

CONCLUSIONS

Morphological changes in the secundines have a limited impact on biometric parameters of neonates from dichorionic twin pregnancies. In turn, functional changes exert a significant effect and more often contribute to impaired fetal development.

Conflict of interest

The authors declare no conflict of interest.

Funding information

The authors have received no funding for this article.

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