

Relationship between type and weight of placenta and neonate birth weight in twin pregnancy

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ABSTRACT: The relationship between the type and size of placenta and the development of twin fetuses is still discussed in perinatology. The objective of this paper is to answer the question whether the final weight and size of placenta is a limiting factor for fetal growth in twin pregnancy. The study material consisted of 1,261 pairs of fetuses from monochorionic (MC) and dichorionic (DC) twin pregnancies, born by cesarean section between pregnancy weeks 22 and 41 at the Perinatology and Gynecology Department of the Poznan University of Medical Sciences between 2003 and 2009. Histological examination of secundines, placental weights, and birth weight of twins were evaluated, and the newborn condition was assessed by the Apgar score. Statistical evaluation by analysis of variance assessed placental growth related to gestational age and also the effect of placental-fetal weight ratio on neonate clinical condition. We observed an increase in placenta growth until 38 weeks of pregnancy in twins sharing one placenta and until 36 weeks of pregnancy in twins with separate placentas. Between 22 and 35 weeks of pregnancy, the placental-fetal weight ratio in twins sharing one placenta was higher and they were also smaller than twins with separate placentas. The placental-fetal weight ratio was comparable in all twins at delivery and was associated with the clinical condition of newborns. Newborns who received an Apgar score of 8 or more 10 minutes post delivery had a lower ratio than neonates with Apgar score equal to or lower than 7 ($p \leq 0.01$). Although these latter twins had both smaller placentas and smaller birth weights, their placental-fetal weight ratios were significantly higher than those of twins born in good condition. Placental growth decreases before pregnancy term but does not limit fetal birth weight in twin pregnancy.

KEY WORDS: twin pregnancy, birth weight, placental-fetal weight ratio, placental weight, separate placentas, single placenta, twins

Introduction

The placenta forms the fetal-placental-maternal unit and as such it influenc-

es the relationship between maternal and fetal organisms. The efficiency of this fetal-placental-maternal unit affects fetal condition and it can provide information

on fetal distress before impaired development and irreversible effects occur.

Two view-points are contrasted in the placental role. The first assumes that the placenta is created jointly by fetus and mother, and depends on the degree of their in-genotypes. The placental size resulting from genetically determined maternal and fetal characteristics is especially attributed to the degree of genetic non-compliance between mother and fetus. A high similarity between maternal and fetal antigens makes immunological recognition of fetal allo-transplants difficult. There is a statistically significant correlation of high similarity between mother and fetus and increased frequency of recurrent miscarriages, trophoblastic diseases and pregnancy induced hypertension (Słomko 1985). Immunological recognition of fetal allo-transplants by the mother stimulates biochemical systems which induce morphological lesions and functional changes in the utero-placental circulation. The placenta is the organ where maternal and fetal regulators meet and control the efficiency of maternal-placental circulation, fetal circulation, and placental membrane functions. Placental adaptive abilities to gestation requirements result in maternal-fetal cooperation (Fox and Sen 1972).

The second point of view stresses that the placenta belongs to the fetus, and its formation depends on fetal genetic properties; where, for example, a small placenta is related to a small fetus (Wallenburg 1971). According to Yu (1992), small birth weight reflects a small placental weight, Decreased placental tissue function results in less perfusion area between mother and fetus, leading to impaired transfer of oxygen and nutrients from mother to fetus. The results of this

study show that fetal growth is confined by the size and function of the placenta. Heinonen et al. (2001) found that placentas in small-for-gestational-age newborns (SGA) were 24% smaller than in appropriate newborn (AGA), and therefore suggested association between fetal growth and placental weight. Similar findings of smaller SGA neonate placentas compared to those in AGA newborns were reported by Kosinska (2004)

The association between fetal weight and placenta size is still under investigation and findings are ambiguous. Fetal development appears to reflect placental size in weight, diameter and functional parameters (Fox 1987). A Norwegian study demonstrated that placental weight is important in determining both fetal development and newborn birth weight, and it also modifies the maternal influence on fetal development and birth weight (Roland et al. 2012). Thame et al. (2001) determined that placental size in the second trimester was a stronger indicator of eventual weight than anthropometric features such as head, abdomen and femur circumferences and the fetal length. They therefore considered this variable a more useful tool for early detection of the risk of small neonate weight. Their further studies registered that both placental size and developmental rate influence fetal growth in the first half of pregnancy (Thame et al. 2004). Jaya et al's 1995 research highlighted the positive correlation between neonate birth weight and placental weight. The study of 2,400 live singleton births confirmed the association of birth and placental weights by linear regression. Here, placental weight determined 36.6% of birth weight variability (Salafia et al. 2008).

Other studies reported that the placenta grows until it reaches functional

maturity regardless of full-term pregnancy length (Hollander i Mart 1968, Granum i Hobbins 1983, Olloffson et al. 1993, Lin et al. 1995), and the fetus can continue growth to delivery regardless of placental growth restrictions.

Our objective is to investigate the association of placental weight and fetal birth weight in twins and to determine if placental size affects neonate birth weight in twin pregnancy.

Materials and methods

The study material consisted of 1,261 pairs of fetuses from monochorionic (MC) and dichorionic (DC) twin pregnancies, born by cesarean section between pregnancy weeks 22 and 41 at the Perinatology and Gynecology Department of Poznan University of Medical Sciences, Poland between 2003 and 2009. Fetuses with twin-to-twin transfusion syndrome were excluded from the study.

The birth weights of twins were measured after delivery and placental weights were assessed during histopathological examination performed at the Obstetrics and Gynaecology Hospital Pathological Laboratory. Secundines were preserved in 10% formalin buffer solution and macroscopic characteristics including dimensions, diameters and weights were assessed following umbilical cord and membrane removal. Individual placental weights for fused-placenta MC twins were obtained by dividing the total placental weight by two. The postnatal condition of newborns, including the five basic clinical features of skin appearance, heart rate, grimace, muscle activity and respiration was evaluated by Apgar score 10 minutes after birth.

The material was analyzed statistically and analysis of variance determined the

relationship between placental weight and gestational age and the correlation between placental-fetal weight ratio and newborn condition. Calculations were performed by Statistica 8 (StatSoft®, Poland), with statistical significance established at $p \leq 0.05$.

Results

Assessment of placental weight during pregnancy is quite challenging, therefore placental weights were routinely estimated after delivery in twins sharing a single placenta and those with individual placentas born between 22 and 41 weeks of pregnancy.

The analysis of our comprehensive neonate research material, including twin placentas, showed that the growth of monochorionic twin placentas increased up to 38 weeks of pregnancy to an average weight of 1,130 g. In contrast, individual placentas in twin pregnancy increased until 36 weeks and the weight was 1,210 g (Table 1). Analysis of variance determined significant correlation between placenta weight in twin pregnancy and gestational age. The *F*-test ratio in single placentas was 15.8 and the sum of individual placentas was 11.5 with a *p*-value of 0.00. The NIR test in Table 2 shows the significance of differences between the weight of the single placenta and the sum of separate placentas in relation to gestational age.

The correlation between birth weight and placental weight is established by the calculation of placental-fetal weight ratios for twins with one placenta and those with two separate placentas.

While the ratio value for twins with separate placentas was calculated according to the formula:

Table 1. Means and standard deviation of placenta weights for twins with single placenta and those with separate placentas, related to gestational age

Gestational age		One placenta		Separate placenta		
Weeks	N	\bar{X}	SD	N	\bar{X}	SD
22	3	420.0	194.7			
23	4	452.5	39.5	1	520.0	0.0
24	1	410.0	0.0	5	466.0	37.8
25	6	465.0	148.2	3	546.7	5.8
26	18	607.8	193.6	5	578.0	104.3
27	15	589.7	159.9	3	750.0	313.2
28	7	775.7	301.3	8	756.3	205.6
29	20	779.0	169.1	7	747.9	260.0
30	18	951.1	239.4	11	771.8	94.8
31	32	835.9	215.9	12	830.8	153.2
32	37	964.1	273.9	21	981.7	198.5
33	52	977.5	253.5	10	1065.5	189.6
34	70	1105.7	267.2	27	1152.0	261.5
35	93	1057.4	229.1	52	1123.9	279.4
36	126	1120.6	286.7	85	1214.2	263.9
37	167	1115.1	238.0	117	1178.3	218.1
38	86	1129.8	242.8	50	1159.5	222.4
39	33	1073.6	183.7	32	1097.8	238.6
40	10	960.0	154.7	7	1131.4	177.3
41	5	978.0	76.9	2	1110.0	70.7

– *placental-fetal weight ratio of twin I = placental weight of twin I/birth weight of twin I*

– *placental-fetal weight ratio of twin II = placenta weight of twin II/birth weight of twin II*

for twins sharing one placenta, this value was the quotient of half the placental weight and birth weight of each twin:

– *placental-fetal weight ratio of twin I = $\frac{1}{2}$ placental weight /birth weight of twin I*

– *placental-fetal weight ratio of twin II = $\frac{1}{2}$ placental weight/birth weight of twin II*

The line chart in Figure 1 highlights the placental-fetal weight ratios of twins with single placenta and separate placentas born between 22 and 41 weeks of pregnancy.

Placental growth is faster than fetal growth in the early stage of pregnancy, and therefore the placental weight is greater than fetal weight at that time. Although the twin's growth is comparable to placental growth during the second trimester, it ultimately surpasses the slowing placental growth rate. After 20 weeks of pregnancy the placental weight is only half that of the fetal weight and this difference increases with gestational age. Placental-fetal weight ratios in our twins born between 36 and 40 weeks of pregnancy ranged between 0.19 and 0.22 (Fig. 1) and this range was higher than the 0.13–0.15 reported by Cieslik (1999 – Fig. 2).

Smaller fetus weights resulted in higher placental-fetal ratio values, and

Table 2. Significance weight differences in single placenta and combined placentas related to gestational age (NIR test results)

		Placental weight																			
		Fetal age from 22 to 41 weeks																			
		22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41
The sum of placental weights	22							*	*	**	**	**	**	**	**	**	**	**	**	**	**
	23	-					*	*	**	**	**	**	**	**	**	**	**	**	**	**	**
	24	-	-				*	*	**	**	**	*	**	**	**	**	**	**	**	**	*
	25	-	-	-			*	**	**	**	**	**	**	**	**	**	**	**	**	**	**
	26	-	-	-	-		*	*	**	**	**	**	**	**	**	**	**	**	**	**	**
	27	-	-	-	-	-		*	*	**	**	**	**	**	**	**	**	**	**	**	**
	28	-	-	-	*			*	*	**	**	*	**	**	**	**	**	**	**	**	**
	29	-	-	-	*	*		*	*	**	**	**	**	**	**	**	**	**	**	**	**
	30	-	-	-	*	*	*		*	*	**	*	**	**	**	**	**	**	**	**	**
	31	-	-	-	**	*	*	*		*	*	*	**	**	**	**	**	**	**	**	**
	32	-	-	-	**	**	**	*	*		*	*	**	**	**	**	**	**	**	**	**
	33	-	-	-	**	**	**	**	**	*	*	*	**	**	**	**	**	**	**	**	**
	34	-	-	-	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
	35	-	-	-	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
	36	-	-	-	**	**	**	**	**	**	**	**	**	*	**	**	**	**	**	**	**
	37	-	-	-	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**
	38	-	-	-	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	*
	39	-	-	-	*	**	**	**	**	**	**	**	**	**	**	*	**	**	**	**	**
	40	-	-	-	**	**	**	*	**	**	**	**	**	**	**	**	**	**	**	**	**
	41	-	-	-	*	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**	**

*significant difference at $p \leq 0.05$ and **at $p \leq 0.01$.

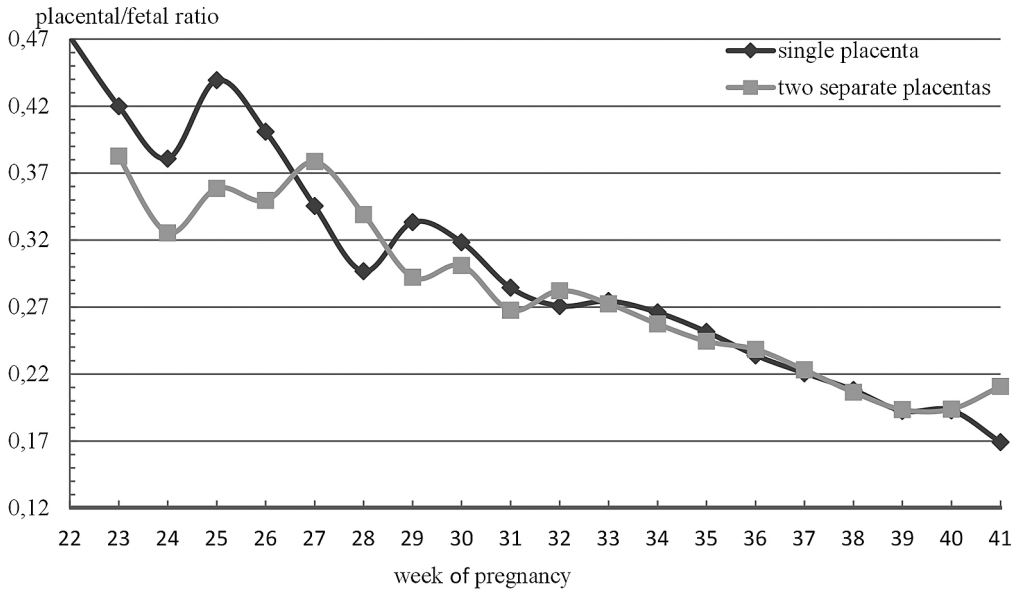


Fig. 1. Placental-fetal weight ratio in combined placenta twins and those with individual placentas

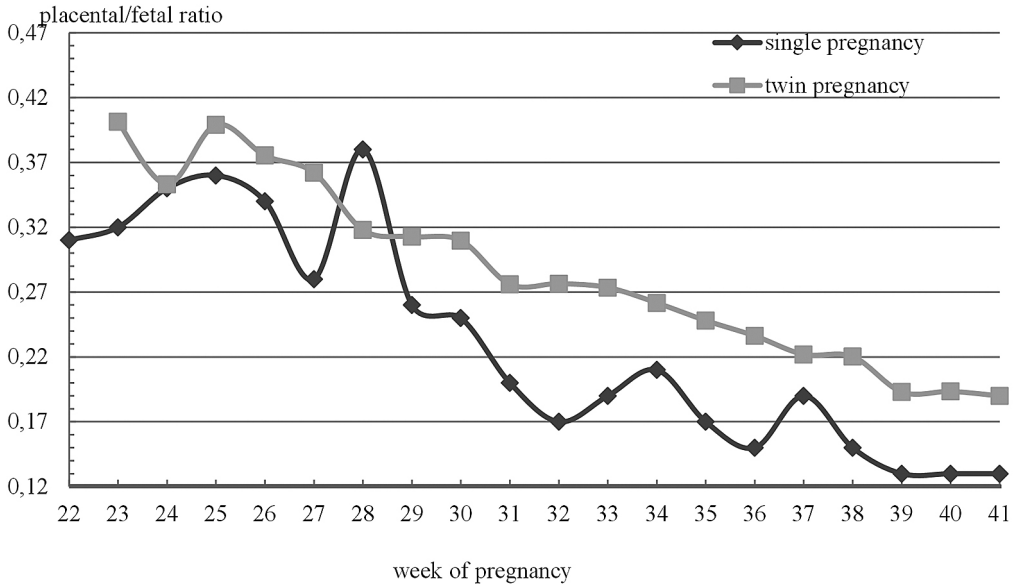


Fig. 2. Placental-fetal weight ratio in twin and singleton pregnancy: singleton pregnancies are according to Cieřlik (1999)

ratios for twins with single placenta versus twins with separate placentas changed according to gestational age so

that they were significantly higher in the former group at 22 to 31 weeks pregnancy. Placental growth slows down after

Table 3. Means and standard deviation of placental-fetal weight ratio, placental weight and birthweight of twins born between 36–38 weeks of pregnancy; related to Apgar score (1, 2) and ANOVA results

Apgar score	N	Placental-fetal weight ratio			Placental weight			Birth weight of twins		
		$\bar{X} \pm SD$	F	p	$\bar{X} \pm SD$	F	p	$\bar{X} \pm SD$	F	p
1 (Apgar \geq 8)	1211	0.22 \pm 0.07	9.6	0.002	1114.7 \pm 248.9	4.0	0.047	2619.0 \pm 416.8	46.1	0.000
2 (Apgar \leq 7)	48	0.26 \pm 0.13			1031.4 \pm 244.6			2131.1 \pm 619.6		

31 weeks pregnancy despite continuous fetal growth and this causes a decrease in placental-fetal ratio in single-placenta twins. Although the placental-fetal ratio of these two twin-groups differs between 31 and 36 weeks pregnancy, the differences are statistically insignificant and comparable after 36 weeks pregnancy (Fig. 1).

We investigated the relationship between placental-fetal weight ratio and newborn condition at birth based on Apgar score for 758 twins with single placenta and 504 twins with separate placentas born between 36 and 38 weeks of pregnancy. The placental-fetal weight ratio was lower in twins with Apgar score ≥ 8 than those with Apgar ≤ 7 10 minutes after birth (Table 3).

The correlation of differences of placental-fetal weight ratios and Apgar score is statistically significant ($p \leq 0.01$) in the analysis of variance (F-ratio of 9.6 has a P-value 0.002). Both placental weights and fetal weights of twins born in general good condition (Ap ≥ 8) are greater compared to twins born in poor condition (Ap ≤ 7).

The ANOVA results are presented in Table 3. The parameter of fetal birth condition at birth assessed in two categories (Apgar ≥ 8 and Apgar ≤ 7) and variances in placental-fetal weight ratio, birth weight and placental weight were analyzed in twins born at 36, 37 and 38 weeks.

Discussion

The placenta is the site of oxygen and nutrient exchange between mother and fetus and therefore has a great impact on fetal birth weight. Placental dimensions related to its weight affect the placental-fetal weight ratio and modify placental function efficiency. Although some compensating fetal mechanisms exist, placental micro- and macroscopic lesions are associated with limitations in fetal growth (Salafia et al. 2006). Saudi Arabian research recorded strong correlation between placental breadth and neonatal body size, and especially birth weight (Alwasel et al. 2012). Both placental volume and growth-rate influence fetal abdominal and head circumferences, femoral length, and the bi-parietal skull diameter at 35 weeks gestation (Thame et al. 2004).

Our study suggests that placental growth slows during the last few weeks of pregnancy. This decrease is neither invariable nor irreversible, so that this type of growth resembles liver growth which consists of long-lived post-mitotic cells. Here, the cells achieve optimal size required for metabolic function while, displaying insignificant residual changes and maintaining great growth reserves.

Previous studies on placental growth reported the following inconsistent results. (1) Hollander and Mart (1968) re-

ported that placental thickness increased until 34 weeks of pregnancy and then total growth stopped. Schlensker (1971), (2) Grannum and Hobbins (1983) registered increased placental thickness until 36 weeks, (3) Molteni (1984) claimed that although placental weight and placental-fetal index increased in AGA and LGA fetuses until 42 weeks of pregnancy, SGA twins had only placental-fetal index increase until that time and their placenta did not change after 36 weeks. (4) Salafia's study of 2,400 subjects, recorded increased placental thickness and birth weight between 34 and 43 weeks. This result contrasted with the placental-fetal weight ratio which decreased at term (Salafia et al. 2007). These differences may result from fetal and placental growth patterns, because while placental growth peak occurs between 28-30 weeks gestational age the fetus grows exponentially until the end of pregnancy (Ananth and VanderWeele 2011); and our findings of decreased placental growth after 31 weeks agree with their conclusion.

Investigated twins delivered in average or poor overall state had significantly higher placental-fetal weight ratio than those born in good condition.

Coall and colleagues (2009) results corroborate our findings that increased placental-fetal weight ratio is associated with restricted intrauterine fetal development, and Ruangvutilert et al. 2002 added that this ratio is associated with unchanging fetal weight in late pregnancy and not with placental hypertrophy

Our study and literature sources indicate that placental weight could not be the lone factor limiting fetal growth. The experimental study on surgical decrease in placental size by Robinson et al. (1979) and the forced artificial increase of oxygen consumption in fetuses re-

ported by Lorijn and Longo (1980) both confirmed that the placenta has functional reserves. In addition, it has been observed that the placenta can increase its volume when necessary. Very large placentas have occurred in pregnant women at high altitude, and also in those with severe anemia and uncompensated heart disease (Iwata et al. 1993).

Although most studies on placental and fetal weight association were conducted in singleton pregnancies, Bleker's twin study in 1995 confirmed a relationship between placental weight and fetal growth, and Eberle et al. (1993) determined that the cause of birth weight differences in DC twins was related to the effect of placental inflammatory lesions and not to different placental weights.

It is commonly claimed that the placenta grows gradually throughout pregnancy and that it attains mature morphological and functional status around the term of delivery. According to some authors, placental villi demonstrate morphological symptoms of aging by the end of pregnancy. This viewpoint is based on misunderstanding and incorrect histological interpretation of both villi maturation processes and the trophoblastic differentiation system. Although it has been suggested that placental aging is a consequence of DNA synthesis cessation at 36 weeks, the total concentration of placental DNA increases linearly until 40-42 weeks (Sand and Dobbing 1985). Flow cytometry confirmed histological evidence of fresh villi formation in the placenta until the end of pregnancy (Fox 1997). This demonstrated continuous DNA synthesis (Iversen and Farsund 1985), and morphological examinations provided evidence of continuous increase in villi area and their progressive branching until term (Boyd 1984).

Conclusion

The results of our studies indicate that placental growth slows during the last few weeks of pregnancy. There appears no reason for further placental growth after it has achieved adequate size for functional efficiency and reserves. Decreased placental-fetal weight ratio in pregnancy demonstrates the continual increase in fetal weight until pregnancy ends. It is beyond doubt that placental size and weight affect fetal weight, but it is highly unlikely that placental weight imposes restrictions on birth weight in the final stages of pregnancy after completion of placental growth

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Author contribution

All authors had substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data. CK and WM drafted the article and revised it critically for important intellectual content. All authors gave their final approval of the version to be published.

Conflict of interest

The authors declare there is no conflict of interests.

All the procedures were approved by the Local Ethics Committee of the Medical University in Poznań.

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