Abruptio placentae – relationship with other placental dysfunction related conditions

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ABSTRACT

Objective: To investigate newborns' sizes associated with abruptio placentae (AP) and to assess the association of a history of pregnancy induced hypertension (PIH) and low birth weight with the occurrence of AP and *vice versa*.
Design: A cohort study based on the Medical Birth Registry of Norway.
Results: AP in the first birth was associated with higher rates of AP, small for gestational age (SGA), and PIH in the second pregnancy. This was particularly evident for early onset preeclampsia (unadjusted odds ratio: 5.9; 95% confidence interval: 3.0–11.5). PIH in the first pregnancy was associated with higher rates of AP in the second. In women who delivered a newborn with weight below the 5th birth weight percentile, AP was 2–3 times more likely to occur than with birth weight percentiles 10–89.9. The occurrence of AP in the second pregnancy also increased with decreasing size at birth in the previous.
Conclusions: A pregnancy subsequent to AP must be considered a risk pregnancy in terms of recurrent AP and excess risk of fetal growth restriction and PIH. In sibships with PIH, fetal growth restriction, or PA among siblings, the risk of AP is increased. This suggests a shared recurrent etiologic factor involving an abnormal feto-maternal relationship in AP, PIH, and fetal growth restriction.

INTRODUCTION

It has been reported that women whose first pregnancy was complicated by small for gestational age (SGA), abruptio placentae (AP), or pregnancy induced hypertension (PIH, preeclampsia and transient hypertension) have increased risk of any of these conditions in the next pregnancy (1,2), and *vice versa* (3). It has been proposed that decidual (placental bed) occlusive vasculopathy, caused by shallow invasion of fetal trophoblasts in the decidual spiral arteries (4,5), tends to recur from one pregnancy to another in the same woman (6). Thus, there is evidence to suggest that SGA, PIH, and AP have a shared etiologic factor which involves placental dysfunction.

An earlier study reported that the risk of SGA in a pregnancy with PIH increased with the severity of PIH (7), which indicates a more important role of placental dysfunction in severe preeclampsia than in the milder subgroups of PIH. Thus, one might expect that the earlier reported association of AP in one pregnancy with PIH in subsequent pregnancies (3) is particularly prevalent in severe PIH and early onset preeclampsia, which indicates severe disease (8).

In December 1998, a revised version of the Medical Birth Registry notification form was implemented to include new variables like data on maternal smoking habits and subgroups of PIH, which are notified by checking of boxes (9). Additionally, possible important confounders such as smoking, maternal age, chronic renal disease, chronic hypertension, rheumatoid arthritis, gestational-, type 1-, and type 2 diabetes are also notified by checking of boxes, which would make adjustments more effective.

The aim of the present study was to investigate newborns' size associated with AP and to assess the association of a history of PIH and low birth weight with the occurrence of AP and *vice versa*.

MATERIALS AND METHODS

Since 1967, all births in Norway are notified to the Medical Birth Registry of Norway based on compulsory notification (9). More than 99% of pregnant women receive standardized antenatal care (10). The registry comprises medical data on all live births and abortions at 16 weeks gestation or more including abortions induced on medical indications. Data are transferred by the midwives to the notification form from the pregnancy record which the women bring to the delivery unit. In December 1998, a revised version of the notification form was implemented to include new variables like data on maternal smoking habits and subgroups of PIH which are notified by checking of boxes (9).

From 1967 till June 2005, 2,236,250 births were

Table 1. Occurrence and recurrence of abruptio placentae (AP).

AP in the first pregnancy	Second pregnancy						
	non-AP (*n*)	AP (*n*)	per 1000	OR	95% CI	OR*	95% CI
no	118528	532	4.5	1		1	
yes	440	18	39.3	9.1	5.6–14.7	8.3	5.1–13.5

* adjusted for smoking, maternal age, chronic renal disease, chronic hypertension, rheumatoid arthritis, gestational-, type 1-, and type 2 diabetes, and interbirth interval

OR: odds ratio; CI: confidence interval

registered. The mothers' national identification number was used to identify 972914 pairs of first and second births. The second birth in each pair of births was restricted to those which occurred from December 1998, when the revised notification form had been introduced. Sibships with multiple births and women with their first births before 1967 were excluded, leaving 119,518 pairs of births for study.

Cases of AP were those births notified as AP to the Medical Birth Registry by plain text, however from December 1998 by a check box. Clinical criteria of PIH in Norway have been in accordance with the recommendations by the American College of Obstetricians and Gynecologists in 1972 (11), which are also referred to in the Medical Birth Registry's instructions for completion of the notification form. Transient hypertension implies pregnancy induced hypertension without proteinuria and with BP ≥ 140/90 (one or both values exceeded) or rise in systolic BP ≥ 30 mmHg or diastolic BP ≥ 15 mmHg after 20 weeks of gestation. Mild preeclampsia implies systolic BP 140–159, diastolic BP 90–109, rise in systolic BP ≥ 30 mmHg, or diastolic BP ≥ 15 mmHg and proteinuria ≥ 1+. Proteinuria is defined as excretion of 0.3 g or more per day, usually equivalent to at least 1+ on a urine reagent strip. Severe preeclampsia implies BP ≥ 160/110 and/or proteinuria ≥ 2+.

According to clinical practice in Norway, pregnancies with edema but without proteinuria are not included in the definition (12). Before December 1998 preeclampsia was recorded in the Medical Birth Registry as one category. Thus, in first pregnancies in the present study PIH was subdivided into preeclampsia and transient hypertension.

The degree of association between e.g. AP in the first pregnancy and PIH in the second were measured by odds ratios (ORs) obtained by logistic regression, in which smoking (yes and no), maternal age (19 or less, 20–29, 30–34, and ≥ 35), chronic renal disease, chronic hypertension, rheumatoid arthritis, gestational-, type 1-, and type 2 diabetes, and interval between births (<1 year, increments of 1 year, 10+ years) were adjusted for. Additionally, in order to indicate the effect of placental dysfunction on the development of AP, the associations between newborn's size and AP was assessed.

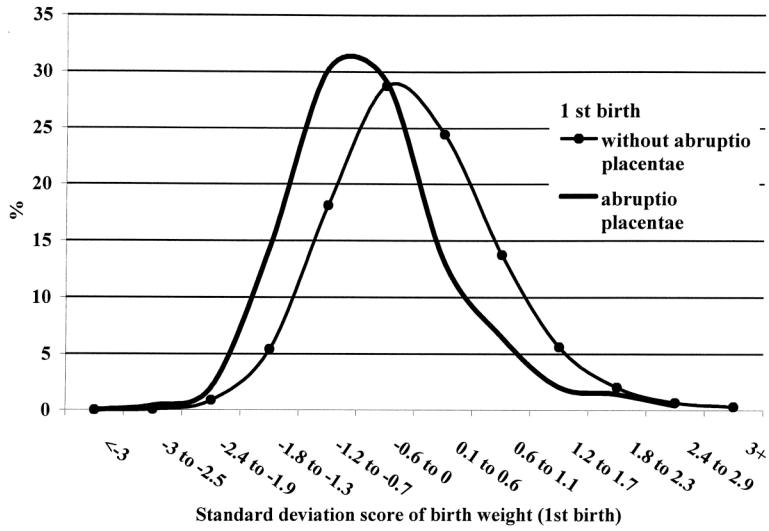
To calculate standard deviation scores (SDSs or z scores) and birth weight percentiles for gestational age, fetal gender, and birth order, birth weight was regressed against gestational age using fractional polynomials (13) and fetal gender was added to the models. For birth order 1 and 2 separate calculations were performed. The method of scaled absolute residuals was used to model SD against gestational age (14). The SDS for each observation was the distance in SDs from the mean regression line. To achieve normal distribution of birth weight, birth weight was power transformed. The statistical analysis was carried out with SPSS (Statistical Package for the Social Sciences, SPSS Inc, Chicago, IL, USA).

RESULTS

In second pregnancies without previous AP, AP occurred in 4.5 per 1000 births, while the recurrence rate was 39.3 per 1000. Crude and adjusted ORs of recurrence were 9.1 and 8.3, respectively (Table 1).

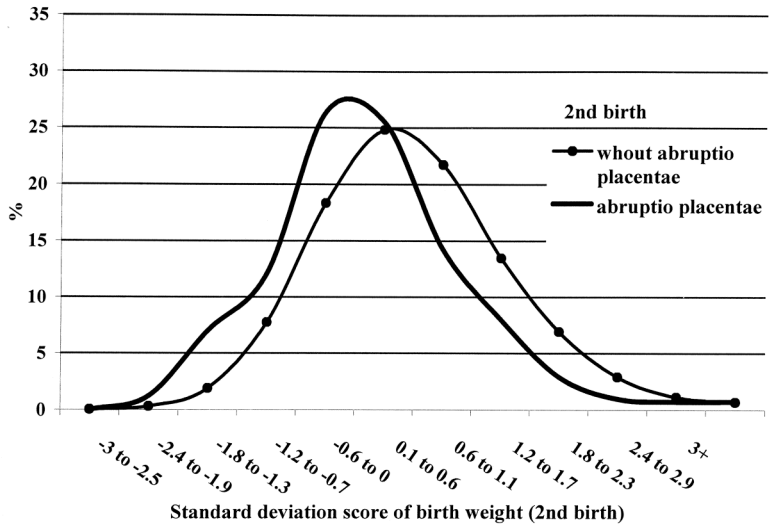
In first as well as second births, women with AP delivered on average significantly lighter infants than those without AP (Figures 1 and 2). Also women with AP in the second delivery delivered on average significantly lighter infants in the first than those without AP (Figure 3) and *vice versa* (Figure 4). In first births the occurrence of AP increased with decreasing birth size (Table 2). In second births the trend was similar. Thus, in women who delivered a newborn with weight below the 5th birth weight percentile, AP was three times more likely to occur than with birth weight percentiles 10–89.9 (adjusted ORs 2.7). The effects of adjusting were small. The occurrence of AP in the second pregnancy also increased with decreasing size at birth in the previous (Table 2). AP in the second pregnancy was two times more likely to occur in women who delivered a newborn with weight below the 5th birth weight percentile in the previous pregnancy (unadjusted ORs 2.0). However, after adjusting this effect was marginal. AP in the first pregnancy increased the rate of SGA (below the 10th birth weight percentile) in the second birth (Table 3). Subsequent to an AP, 14.3% had SGA compared with 8.3% subsequent to a non-SGA birth (unadjusted OR: 1.8).

PIH in the first pregnancy was associated with about a twofold excess rate of AP in the second, with unadjusted ORs for transient hypertension and preeclampsia of 1.7 and 1.9, respectively (Table 4). The effects of adjusting were negligible. However, the



Abruptio placentae	Standard deviation score			
	mean	95% CI		*p* -value
no	0.002	-0.003	0.007	<0.0001
yes	-0.462	-0.539	-0.386	

Figure 1. Distribution of newborn's size (standard deviation scores) in first births with and without abruptio placentae.



Abruptio placentae	Standard deviation score			
	mean	95% CI		*p* -value
no	0.002	-0.004	0.008	<0.0001
yes	-0.439	-0.536	-0.341	

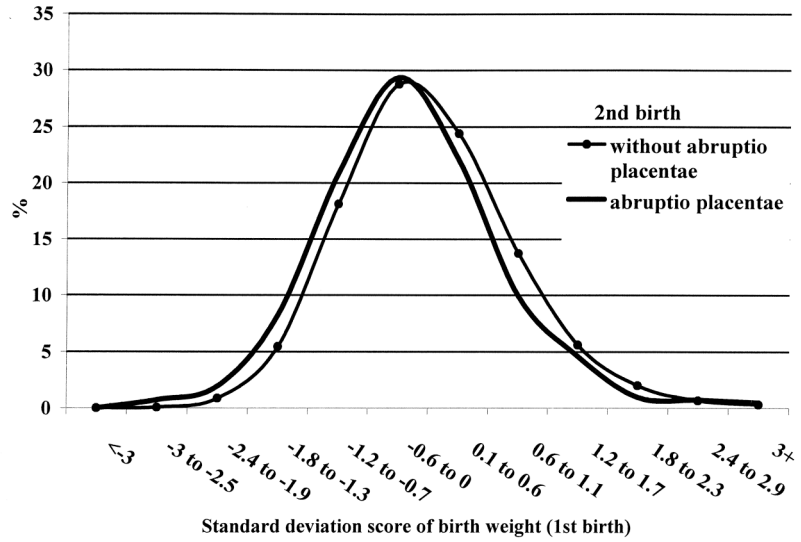
Figure 2. Distribution of newborn's size (standard deviation scores) in second births with and without abruptio placentae.

association with transient hypertension was not significant.

Women with AP in the first birth had excess rates of PIH in the second (Table 5). The association increased with severity of PIH. Transient hypertension was 20% more likely to occur after AP in the first. However, the association was not significant. Subsequent to an AP birth, mild and severe preeclampsia were two-three times more likely to occur (unadjusted ORs=2.5 and 2.9, respectively), while early onset preeclampsia was six-fold increased (unadjusted OR=5.9; 95% confidence interval: 3.0–11.5).

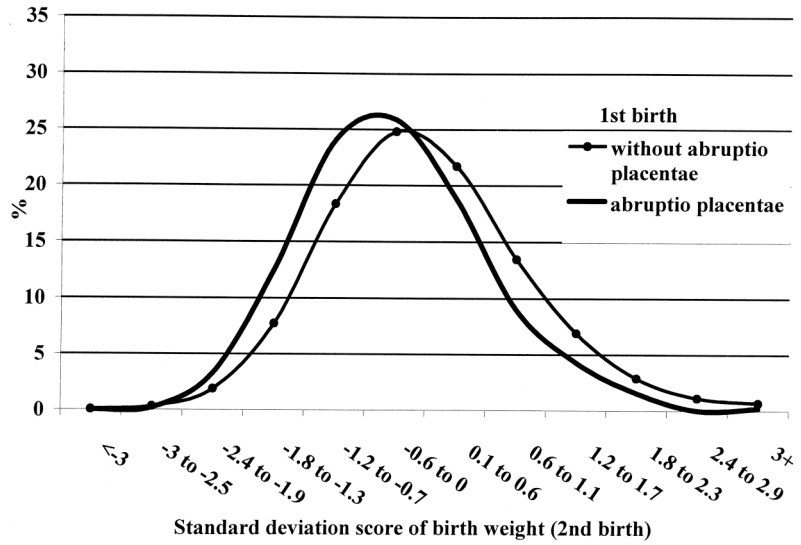
DISCUSSION

AP in the first delivery was associated with higher rates of AP, SGA, and PIH in the second. This was particularly evident for early onset preeclampsia. PIH in the first birth was associated with higher rates of AP in the second. In women who delivered a newborn



Abruptio placentae	Standard deviation score			
	mean	95% CI		*p*-value
no	0.001	-0.005	0.006	<0.0001
yes	-0.157	-0.241	-0.074	

Figure 3. Distribution of newborn's size (standard deviation scores) in first births in women with and without abruptio placentae in the second.



Abruptio placentae	Standard deviation score			
	mean	95% CI		*p*-value
no	0.001	-0.004	0.007	<0.0001
yes	-0.317	-0.405	-0.230	

Figure 4. Distribution of newborn's size (standard deviation scores) in second births in women with and without abruptio placentae in the first.

with weight below the 5th birth weight percentile, AP was 2–3 times more likely to occur. The occurrence of AP in the second birth also increased with decreasing size at birth in the previous.

An association between a pregnancy complication recorded in the previous delivery notification chart, without knowledge of future birth outcomes, and future birth outcomes recorded in the current delivery would not be affected by a recall bias. The estimates are therefore considered reliable. Another strength of the present study was the ability to adjust for possible important confounders. However, the effects of adjusting were small.

The results of the present study confirm those of earlier studies on recurrence of AP (15,16), the association of SGA and PIH with AP in later pregnancies

Table 2. Abruptio placentae in the first or second pregnancy by birth weight percentiles in the first or second birth.

Birth weight		Abruptio placentae					
percentiles	Total (*n*)	*N*	%	OR	95% CI	OR*	95% CI
First birth		First pregnancy					
<5	1816	20	1.1	2.8	1.8–4.4	2.7	1.7–4.1
5–9.9	3753	40	1.2	2.5	1.8–3.5	2.4	1.7–3.4
10–89.9	96057	412	0.4	1		1	
90–94.9	3858	8	0.2	0.5	0.2–1.0	0.5	0.3–1.0
95+	4351	9	0.2	0.5	0.2–0.9	0.5	0.3–0.9
Second birth		Second pregnancy					
<5	3791	40	1.1	3.0	2.2–4.2	2.7	2.0–3.8
5–9.9	5519	34	0.6	1.8	1.2–2.5	1.6	1.2–2.3
10–89.9	90377	317	0.4	1		1	
90–94.9	4859	8	0.2	0.5	0.2–0.9	0.5	0.2–1.0
95+	6656	12	0.2	0.5	0.3–0.9	0.5	0.3–0.9
First birth		Second pregnancy					
<5	1816	13	0.7	2.0	1.1–3.5	1.8	1.0–3.1
5–9.9	3753	24	0.6	1.8	1.2–2.7	1.7	1.1–2.5
10–89.9	96057	347	0.4	1		1	
90–94.9	3858	16	0.4	1.1	0.7–1.9	1.2	0.7–2.0
95+	4351	12	0.3	0.8	0.4–1.4	0.7	0.4–1.4

* adjusted for smoking, maternal age, chronic renal disease, chronic hypertension, rheumatoid arthritis, gestational-, type 1-, and type 2 diabetes, and interbirth interval

OR: odds ratio; CI: confidence interval

Table 3. Birth weight percentile <10 in the second birth according to abruptio placentae (AP) in the first.

AP in the first	Below the 10th weight percentile in the second pregnancy						
pregnancy	non-AP (*n*)	AP (*n*)	%	OR	95% CI	OR*	95% CI
no	101044	9237	8.3	1		1	
yes	436	74	14.3	1.8	1.4–2.4	1.7	1.4–2.2

* adjusted for smoking, maternal age, chronic renal disease, chronic hypertension, rheumatoid arthritis, gestational-, type 1-, and type 2 diabetes, and interbirth interval

OR: odds ratio; CI: confidence interval

Table 4. Abruptio placentae (AP) in the second pregnancy by pregnancy induced hypertension in the first.

	Second pregnancy						
First pregnancy	Non-AP	AP	per 1000	OR	95% CI	OR*	95% CI
Transient hypertension							
no	117037	445	3.8	1		1	
yes	2023	13	6.4	1.7	0.97–2.9	1.7	0.97–3.0
Preeclampsia							
no	112973	416	3.7	1		1	
yes	6087	42	6.9	1.9	1.4–2.6	1.9	1.4–2.6

* adjusted for smoking, maternal age, chronic renal disease, chronic hypertension, rheumatoid arthritis, gestational-, type 1-, and type 2 diabetes, and interbirth interval

OR: odds ratio; CI: confidence interval

Table 5. Pregnancy induced hypertension (PIH) in the second pregnancy by abruptio placentae (AP) in the first.

AP in the first		PIH in second pregnancy						
pregnancy	Total (*n*)	Type of PIH	*n*	per 1000	OR	95% CI	OR*	95% CI
no	118968	Transient hypertension	1642	13.8	1		1	
yes	550		9	16.4	1.2	0.6–2.3	1.1	0.6–2.2
no	118968	Mild preeclampsia	2190	18.4	1			
yes	550		25	45.5	2.5	1.7–3.8	2.4	1.6–3.6
no	118968	Severe preeclampsia	747	6.3	1		1	
yes	550		10	18.2	2.9	1.6–5.5	2.7	1.4–5.1
no	118968	Early onset preeclampsia	335	2.8	1		1	
yes	550		9	16.4	5.9	3.0–11.5	5.3	2.7–10.4

* adjusted for smoking, maternal age, chronic renal disease, chronic hypertension, rheumatoid arthritis, gestational-, type 1-, and type 2 diabetes, and interbirth interval

OR: odds ratio; CI: confidence interval

(1), and *vice versa* (3,17). However, in previous studies lack of data did not allow subdivision into all categories of PIH. The result in the present study that small newborn size was associated with AP is also consistent with earlier studies (18,19).

In the present study, the association of AP in the first pregnancy with PIH in the subsequent one increased with severity of PIH. For early onset preeclampsia, indicating severe disease (8), the association was markedly increased (crude and adjusted ORs 5.9 and 5.3, respectively). This indicates a more important role of placental dysfunction in severe PIH, and in particular early onset preeclampsia, than in the milder subgroups of PIH. These results are consistent with earlier reports to the effect that the risk of SGA in a pregnancy with PIH increased with the severity of PIH (7) and that early diagnosis of preeclampsia tripled the recurrence risk (8). They also agree with a study reporting that preterm preeclampsia was associated with lighter, shorter, and leaner newborns, whereas late preeclampsia had increased rates of both smaller and larger newborns (20). Additionally, morphological studies on preeclampsia (21,22) and fetal growth restriction (21,23) have reported placental dysfunction-related occlusive lesions in the spiral arteries such as fibrinoid necrosis or acute atherosis. Thus, the lesions are unlikely to be specific, and the conditions mentioned (AP, fetal growth restriction, and PIH) may share pathophysiological factors. The results of the present study thus support the hypothesis that the conditions may represent different clinical expressions of a recurring placental dysfunction. The earlier reported association between SGA in the first birth and subsequent preeclampsia (2) also supports this hypothesis.

In conclusion, a pregnancy subsequent to AP must be considered a risk pregnancy in terms of recurrent AP and excess risk of fetal growth restriction and PIH. In sibships with PIH, fetal growth restriction, or AP among siblings, the risk of AP is increased. This suggests a shared recurrent etiologic factor involving an abnormal feto-maternal relationship in AP, PIH, and fetal growth restriction.

REFERENCES

1. Rasmussen S, Irgens LM, Dalaker K. A history of placental dysfunction and risk of placental abruption. *Paediatr Perinat Epidemiol* 1999; **13**: 9-21.
2. Rasmussen S, Irgens LM, Albrechtsen S, Dalaker K. Predicting preeclampsia in the second pregnancy from low birth weight in the first pregnancy. *Obstet Gynecol* 2000; **96**: 696-700.
3. Rasmussen S, Irgens LM, Dalaker K. Outcome of subsequent pregnancies after placental abruption: a risk assessment. *Acta Obstet Gynecol Scand* 2000; **79**: 496-501.
4. Robertson WB, Brosens I, Dixon HG. The pathological vascular response of the vessels of the placental bed to hypertensive pregnancy. *J Pathol Bacteriol* 1967; **93**: 581-92.
5. Khong TY, De Wolf F, Robertson WB, Brosens I. Inadequate maternal vascular response to placentation in pregnancies complicated by preeclampsia and by small-for-gestational age infants. *Br J Obstet Gynaecol* 1986; **93**: 1049-59.
6. Redline RW. Placenta and adnexa in late pregnancy. In: Reed CB, Claireaux GB, Cockburn F, ed. Diseases of the fetus and newborn. Pathology, imaging, genetics and management. London: Chapman & Hall Medical, 1995: 328-34.

7. Rasmussen S, Irgens LM. The effects of smoking and hypertensive disorders on fetal growth. *BMC Pregnancy Childbirth* 2006; **6**: 16.
8. Hjartardottir S, Leifsson BG, Geirsson RT, Steinthorsdottir V. Recurrence of hypertensive disorder in second pregnancy. *Am J Obstet Gynecol* 2006; **194**: 916-20.
9. Irgens LM. The Medical Birth Registry of Norway. Epidemiological research and surveillance throughout 30 years. *Acta Obstet Gynecol Scand* 2000; **79**: 435-9.
10. Backe B. Overutilization of antenatal care in Norway. *Scand J Public Health* 2001; **29**: 129-32.
11. National High Blood Pressure Education Program Working Group. High blood pressure in pregnancy. *Am J Obstet Gynecol* 1990; **163**: 1691-712.
12. Øian P, Henriksen T, Sviggum O. Norwegian Society of Obstetrics and Gynecology. Clinical guidelines in obstetrics. Hypertension in pregnancy. In: Dalaker K, Berle EJ, eds. Oslo, Norway: The Norwegian Medical Association, 1999; 101-2.
13. Altman DG, Chitty LS. Charts of fetal size: 1. Methodology. *Br J Obstet Gynaecol* 1994; **101**: 29-34.
14. Royston P, Wright EM. How to construct 'normal ranges' for fetal variables. *Ultrasound Obstet Gynecol* 1998; **11**: 30-8.
15. Kåregård M, Gennser G. Incidence and recurrence rate of abruptio placentae in Sweden. *Obstet Gynecol* 1986; **67**: 523-8.
16. Rasmussen S, Irgens LM, Dalaker K. The effect on the likelihood of further pregnancy of placental abruption and the rate of its recurrence. *Br J Obstet Gynaecol* 1997; **104**: 1292-5.
17. Matsaseng T, Bagratee JS, Moodley J. Pregnancy outcomes in patients with previous history of abruptio placentae. *Int J Gynecol Obstet* 2006; **92**: 253-4.
18. Rasmussen S, Irgens LM, Bergsjø P, Dalaker K. The occurrence of placental abruption in Norway 1967-1991. *Acta Obstet Gynecol Scand* 1996; **75**: 222-8.
19. Ananth CV, Berkowitz GS, Savitz DA, Lapinski RH. Placental abruption and adverse perinatal outcomes. *JAMA* 1999; **282**: 1646-51.
20. Rasmussen S, Irgens LM. Fetal growth and body proportion in preeclampsia. *Obstet Gynecol* 2003; **101**: 575-83.
21. Sheppard BL, Bonnar J. An ultrastructural study of utero-placental spiral arteries in hypertensive and normotensive pregnancy and fetal growth retardation. *Br J Obstet Gynaecol* 1981; **88**: 695-705.
22. Robertson WB, Khong TY, Brosens I, De Wolf F, Sheppard BL, Bonnar J. The placental bed biopsy: review from three European centers. *Am J Obstet Gynecol* 1986; **155**: 401-12.
23. De Wolf F, Brosens I, Renaer M. Fetal growth retardation and the maternal arterial supply of the human placenta in the absence of sustained hypertension. *Br J Obstet Gynaecol* 1980; **87**: 678-85.