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Twin chorionicity and pre-eclampsia

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ABSTRACT

Objective *To determine whether the incidence of pre-eclampsia is different in dichorionic compared to monochorionic twin pregnancies.*

Methods *The study involved 666 twin pregnancies resulting in two live births after 24 weeks of gestation. Ultrasound examination at 10–14 weeks of gestation demonstrated that 171 (25.7%) were monochorionic and 495 (74.3%) were dichorionic twins. Pregnancy outcome information regarding the development of pre-eclampsia was obtained from the maternity units. The incidence of pre-eclampsia in the dichorionic and monochorionic twin pregnancies was compared.*

Results *The incidence of pre-eclampsia in monochorionic twin pregnancies (9.4%) was not significantly different from that in dichorionic pregnancies (7.3%) (*P = *0.48). Multiple logistic regression revealed that chorionicity has no effect on the development of pre-eclampsia after adjusting for maternal age, ethnic group, maternal smoking, parity and gestational age at delivery (*P = *0.6; odds ratio for monochorionic compared with dichorionic twin pregnancies, 1.19; 95% confidence interval, 0.61–2.3).*

Conclusion *In twin pregnancies chorionicity does not affect the incidence of pre-eclampsia.*

INTRODUCTION

The incidence of pre-eclampsia (PE) is increased in twin compared to singleton pregnancies and has been reported to be in the range of 6–31%[1–3]. It has been suggested that hypertensive disorders in pregnancy are related to the immunological differences between the mother and the fetus but studies examining the association of PE with sex or zygosity have given conflicting results[1,4–10]. Zygosity can be determined accurately only by examination of DNA markers, which implies invasive testing prenatally[11]. Consequently, even if the information on the incidence of PE in the different types of twins was accurate, it precludes this method from routine application. On the other hand, determination of chorionicity can be performed reliably and non-invasively during the first trimester of pregnancy[12] which makes this method a useful tool for counseling pregnant women prenatally regarding the risk of PE.

We investigated the incidence of PE in twin pregnancies in relation to chorionicity, as assessed by first-trimester ultrasound examination.

MATERIALS AND METHODS

At King's College Hospital, women are offered screening for chromosomal abnormalities from a combination of maternal age and fetal nuchal translucency thickness at 10–14 weeks of gestation[13]. Demographic characteristics including maternal age, ethnic group, smoking, parity and ultrasound findings are entered into a computer database at the time of scanning. Twin pregnancies are classified as dichorionic or monochorionic according to the presence or absence of an extension of placental tissue into the base of the intertwin membrane, visualized by sonography as the λ-sign and T-sign, respectively[12]. Gestational age is determined on the basis of the last menstrual period or, if this is uncertain, on the basis of the measurement of the crown–rump length of the larger fetus.

A computer search was conducted for twin pregnancies with live fetuses at 10–14 weeks of gestation that had been seen in our department between September 1996 and September 1999. Only pregnancies that resulted in two liveborns after 24 weeks of gestation were included. Pregnancy outcome information was obtained from the maternity units. Pre-eclampsia was defined according to the classification of the International Society for the Study of Hypertension in Pregnancy[14]. Women with chronic hypertension, renal disease or diabetes were excluded. Variables considered to be of potential importance in the analysis included maternal age, ethnic group, maternal smoking, parity and gestational age at delivery.

Statistical analysis was performed using Statistical Package for Social Sciences (Chicago, IL, USA, version 8). The chi-square test and univariate logistic regression were used to determine

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the significance of differences between twin pregnancies that developed PE and those that did not in terms of maternal age, ethnic group, maternal smoking, parity, gestational age at delivery and chorionicity or zygosity. The gestational age at delivery was divided into quartiles, as there was evidence that it was not associated linearly with the risk of PE. Multiple logistic regression analysis was performed using as outcome the presence or absence of PE and as determinants all of the above factors. Odds ratios (ORs) and 95% confidence intervals (95% CIs) are reported.

RESULTS

The study consisted of data on 666 twin pregnancies, with known chorionicity, identified at 10–14 weeks of gestation and resulting in two live births after 24 weeks of gestation. There were no significant differences between those pregnancies that developed PE and those that did not in any of the variables examined apart from the gestational age at delivery (Table 1). The incidence of PE in monochorionic and dichorionic twin pregnancies was 9.4% (95% CI, 5–13%) and 7.3% (95% CI, 5–9.6%), respectively. Multiple logistic regression revealed that chorionicity did not have any effect on the development of PE after adjusting for maternal age, ethnic group, maternal smoking, parity and gestational age at delivery ($P = 0.6$; OR for monochorionic compared to dichorionic twin pregnancies, 1.19; 95% CI, 0.61–2.31).

Knowing that all dichorionic twin pregnancies resulting in two different-sex liveborns are definitely dizygotic and that all monochorionic twin pregnancies are definitely monozygotic[11], we also decided to investigate if the zygosity had any effect on the risk of PE. There were 394 twin pregnancies (223 dizygotic and 171 monozygotic). There were no significant differences between those pregnancies that developed PE and those that did not in any of the variables examined apart from the gestational age at delivery (Table 2). Multiple logistic regression revealed that zygosity did not have any effect on the development of PE after adjusting for maternal age, ethnic group, maternal smoking, parity and gestational age at delivery ($P = 0.48$; OR for dizygotic compared to monozygotic twin pregnancies, 1.29; 95% CI, 0.62–2.71).

DISCUSSION

This study demonstrates that the incidence of PE is similar in monochorionic and dichorionic twin pregnancies. The rate of PE observed in this study is within the wide range previously reported for twin pregnancies, which varies from 6 to 31%[1–3].

Previous studies investigating the incidence of PE in relation to zygosity in twin pregnancies have given conflicting results with incidence of PE in monozygotic twins being reported as higher, similar or lower compared to dizygotic twin pregnancies[1,4–10]. These differences may be due to the fact that in the majority of the studies the determination of zygosity was based on the sex of the fetuses using Weinberg's hypothesis that for every pair of unlike-sex dizygotic twins there will be one like-sex pair[15]. Consequently, these studies could not determine zygosity accurately and their methods can only give approximate results. However, some studies have used accurate methods of determining the zygosity such as placental histology, blood groups, red cell and placental enzymes of the offspring and HLA typing of the like-sex twins[6–10]. The majority of these studies showed the incidence of PE in monozygotic twins to be similar to that in dizygotic twins, as in our study. However, many of these studies are not recent and extend over a long period of time, and hence the definition of PE used varies markedly. The only study[10] that has investigated the relationship of chorionicity with PE, which was a total population study of twin pregnancies, demonstrated that the incidence of PE was significantly

Table 1 Comparison of demographic characteristics, chorionicity and gestational age at delivery in 666 twin pregnancies according to the development of pre-eclampsia

Characteristic	*Pre-eclampsia* (n = *52*)	*No pre-eclampsia* (n = *614*)	P	*Odds ratio* (*95% CI*)
Maternal age (years) (median (range))	34 (28–37)	33 (29–37)	0.89	(0.94–1.05)
Ethnic group			0.79	
Afro-Caribbean (*n* (%))	11 (9.3)	107 (90.7)		
Caucasian (*n* (%))	39 (7.5)	480 (92.5)		0.79 (0.39–1.59)
Other (*n* (%))	2 (6.9)	27 (93.1)		0.72 (0.15–3.45)
Smoking			0.37	
Smokers (*n* (%))	6 (5.3)	107 (94.7)		
Non-smokers (*n* (%))	46 (8.3)	507 (91.7)		1.62 (0.67–3.89)
Parity			0.16	
Parous (*n* (%))	23 (6.3)	340 (93.7)		
Nulliparous (*n* (%))	29 (9.6)	274 (90.4)		1.56 (0.88–2.77)
Chorionicity			0.48	
Dichorionic (*n* (%))	36 (7.3)	459 (92.7)		
Monochorionic (*n* (%))	16 (9.4)	155 (90.6)		1.32 (0.71–2.44)
GA at delivery (weeks) (median (range))	35.5 (34–36)	37 (35–38)	0.003	
38–41 weeks (*n* (%))	7 (4.1)	162 (95.9)		
36–37 weeks (*n* (%))	7 (4)	168 (96)		0.96 (0.33–2.81)
34–35 weeks (*n* (%))	22 (13.7)	139 (86.3)		3.66 (1.51–8.83)
24–33 weeks (*n* (%))	16 (9.9)	145 (90.1)		2.55 (1.02–6.38)

GA, gestational age.

Table 2 Comparison of demographic characteristics, zygosity and gestational age at delivery in 394 twin pregnancies according to the development of pre-eclampsia

Characteristic	*Pre-eclampsia* (n = *41*)	*No pre-eclampsia* (n = *353*)	P	*Odds ratio* (*95% CI*)
Maternal age (years) (median (range))	34 (28.5–37)	33 (30–37)	0.92	(0.94–1.06)
Ethnic group			0.32	
Afro-Caribbean (*n* (%))	10 (15.6)	54 (84.4)		
Caucasian (*n* (%))	29 (9.3)	284 (90.7)		0.55 (0.25–1.19)
Other (*n* (%))	2 (11.8)	15 (88.2)		0.72 (0.14–3.65)
Smoking			0.18	
Smokers (*n* (%))	3 (4.8)	59 (95.2)		
Non-smokers (*n* (%))	38 (11.4)	294 (88.6)		2.54 (0.76–8.5)
Parity			0.37	
Parous (*n* (%))	20 (9)	203 (91)		
Nulliparous (*n* (%))	21 (12.3)	150 (87.7)		1.42 (0.75–2.71)
Zygosity			0.91	
Monozygotic (*n* (%))	17 (9.9)	154 (90.1)		
Dizygotic (*n* (%))	24 (10.8)	199 (89.2)		1.09 (0.57–2.11)
GA at delivery (weeks) (median (range))	35 (33.5–36)	36 (34–37)	0.008	
38–41 weeks (*n* (%))	4 (4.5)	85 (95.5)		
36–37 weeks (*n* (%))	5 (5.1)	94 (94.9)		1.13 (0.29–4.35)
34–35 weeks (*n* (%))	17 (18.1)	77 (81.9)		4.69 (1.51–14.55)
24–33 weeks (*n* (%))	15 (13.4)	97 (86.6)		3.28 (1.05–10.28)

GA, gestational age.

higher in monochorionic compared to dichorionic twin pregnancies (20.5% vs. 14.4%, $P < 0.05$). However, in this study the investigators did not adjust for other variables, which can affect the incidence of PE, such as maternal age, ethnic group and maternal smoking[3,16]. Moreover, the incidence of PE reported was different from the one found in the present study, suggesting that the two studies are not directly comparable.

In the present study we have examined the relationship of chorionicity in twin pregnancies with PE rather than the association of zygosity with PE. Zygosity can be determined accurately only by examination of DNA markers[11]. Prenatally, such testing would require an invasive procedure to sample amniotic fluid (amniocentesis), placental tissue (chorionic villus sampling) or fetal blood (cordocentesis)[11]. Thus, even if we had accurate information regarding the association of zygosity with PE this would not be a useful tool for prenatally counseling women with twin pregnancies regarding the risk of PE. On the contrary, determination of chorionicity can be performed reliably and non-invasively during the first trimester of pregnancy by sonographic examination of the base of the intertwin membrane for the presence or absence of the lambda sign[12].

It has been hypothesized that immunoincompatibility between mother and fetus contributes to the pathogenesis of PE[17]. If this were the case, the incidence of PE should be higher in dizygotic compared to monozygotic twin pregnancies and similar in monozygotic twin and singleton pregnancies. Since one third of monozygotic twins are dichorionic and about 10% of dichorionic twins are monozygotic[11] it would be anticipated that the incidence of PE would be higher in dichorionic compared to monochorionic twin pregnancies. The present study has demonstrated that the incidence of PE is similar in both types of twins and consequently is not supportive of the above concept. Therefore, it could be hypothesized that the higher immunological load, as the increased placental mass in twin compared to singleton pregnancy implies, rather than the greater fetomaternal antigenic differences, could contribute to the increased incidence of PE observed in this population.

In summary, we have shown that the incidence of PE is similar in dichorionic and monochorionic twin pregnancies. This information can be used to prenatally counsel pregnant women with twin pregnancies.

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REFERENCES

1 McFarlane A, Scott JS. Pre-eclampsia/eclampsia in twin pregnancies. *J Med Genet* 1976; 13: 208–11
2 Bulfin MJ, Lawler PE. Problems associated with toxemia in twin pregnancies. *Am J Obstet Gynecol* 1957; 73: 37–42
3 Coonrod DV, Hickok DE, Zhu K, Easterling TR, Daling JR. Risk factors for preeclampsia in twin pregnancies: a population-based cohort study. *Obstet Gynecol* 1995; 85: 645–50
4 Stevenson AC, Davison BC, Say B, Ustuoplu S, Liya D, Abul-Einen M, Toppozada HK. Contribution of fetal/maternal incompatibility to aetiology of pre-eclamptic toxaemia. *Lancet* 1971; 2: 1286–9
5 Stevenson AC, Say B, Ustaoglu S, Durmus Z. Aspects of pre-eclamptic toxaemia of pregnancy, consanguinity, twinning in Ankara. *J Med Genet* 1976; 13: 1–8
6 Starkie CM, Crawford JS. Twins, immuno-incompatibility and pre-eclampsia. *Int J Gynaecol Obstet* 1976; 14: 559–60
7 Campbell DM, MacGillivray I, Thompson B. Twin zygosity and pre-eclampsia. *Lancet* 1977; 2: 97
8 McMullan PF, Norman RJ, Marivate M. Pregnancy-induced hypertension in twin pregnancy. *Br J Obstet Gynaecol* 1984; 91: 240–3
9 Santema JG, Koppelaar I, Wallenburg HC. Hypertensive disorders in twin pregnancy. *Eur J Obstet Gynecol Reprod Biol* 1995; 58: 9–13

10 Campbell DM, MacGillivray I. Preeclampsia in twin pregnancies. incidence and outcome. *Hypertens Pregnancy* 1999; 18: 197–207
11 Nicolaides KH, Sebire NJ, Snijders RJM. Multiple pregnancy. In: Nicolaides KH, ed. *The 11–14-Week Scan. The Diagnosis of Fetal Abnormalities*. Carnforth: Parthenon Publishing, 1999: 149–85
12 Sepulveda W, Sebire NJ, Hughes K, Odibo A, Nicolaides KH. The lambda sign at 10–14 weeks of gestation as a predictor of chorionicity in twin pregnancies. *Ultrasound Obstet Gynecol* 1996; 7: 421–3
13 Snijders RJM, Noble P, Sebire N, Souka A, Nicolaides KH. UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal-translucency thickness at 10–14 weeks of gestation. Fetal Medicine Foundation First Trimester Screening Group. *Lancet* 1998; 352: 343–6
14 Davey DA, MacGillivray I. The classification and definition of the hypertensive disorders of pregnancy. *Am J Obstet Gynecol* 1988; 158: 892–8
15 Weinberg W. Differenzmethode und Geburtenfolge bei Zwillingen. *Genetica* 1934; 16: 282–8
16 Sibai BM, Ewell M, Levine RJ, Klebanoff MA, Esterlitz J, Catalano PM, Goldenberg RL, Joffe G. Risk factors associated with preeclampsia in healthy nulliparous women. *Am J Obstet Gynecol* 1997; 177: 1003–10
17 Stevenson AC, Davison BC, Say B, Ustuoplu S, Liya D, Abul-Einen M, Toppozada HK. Contribution of fetal/maternal incompatibility to aetiology of pre-eclamptic toxaemia. *Lancet* 1971; 2: 1286–9