Prediction of Spontaneous Preterm Delivery in Twin Pregnancies By Cervical Length at Mid-Gestation

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The objective of our study was to evaluate the correlation of the cervical length at 20–25 weeks of gestation with the incidence of spontaneous preterm delivery in twins in a country with a high incidence of preterm delivery compared to other European countries. Cervical length was measured in 262 consecutive patients. Previous preterm delivery before 34 weeks of gestation, chorionicity, maternal age, body-mass-index, smoking habit and parity were recorded as risk factors for preterm delivery. Women who were symptomatic at 20–25 weeks and who delivered because of other reasons than spontaneous labour and preterm rupture of membranes or at term were excluded. The primary outcome was incidence of preterm birth before 34 weeks. Two hundred and twenty-three patients were analyzed. Thirty-two (14%) delivered before 34 weeks. There was a significant correlation between cervical length of less than 25 mm and spontaneous delivery before 34 weeks (50% vs. 13%, $p = .007$). In addition, logistic regression analysis found cervical length to be the only significant predictor of spontaneous delivery before 34 weeks (OR 1.084; 95% CI 1.015; 1.159; $p = .017$). We conclude that the risk of severe preterm delivery in twins is high. Cervical length at mid-gestation was the only predictor of delivery before 34 weeks.

Keywords: preterm delivery, twin pregnancy, measurement of the cervical length

The incidence of preterm delivery has not decreased in the last decades, despite of advances in medical care. Preterm delivery remains the largest factor of perinatal mortality and morbidity (Guyer et al., 1997). Mortality is more than 90% for infants born at 23 weeks of gestation and declines to 2% for those born at 32 weeks (Draper et al., 1999; Guyer et al., 1997). In addition, preterm birth is a financial burden to the health service due to the costs for neonatal intensive care and long-term support (Petrou, 2005). Nearly one half of all children born before 26 completed weeks of gestation are severely disabled (Wood et al., 2000).

Preterm delivery is defined as birth before 37 weeks of pregnancy; however, births before 34 weeks of gestation account for most neonatal deaths and morbidities. The rate of spontaneous delivery is much higher in twin compared to singleton pregnancies. About 1 to 3% of singleton pregnancies are born before 34 weeks of gestation, and 12% of twin pregnancies (Martin et al., 2006; Statistik Austria, 2005). Multiple pregnancies therefore account overall for about one-fourth of all infants born at less than 34 weeks (Statistik Austria, 2005). In Europe, wide variations in rates of preterm deliveries were found between countries, Austria showing the highest rate of preterm deliveries in twin pregnancies (Blondel et al., 2006).

In singleton pregnancies, risk factors for spontaneous preterm delivery are low body-mass-index, smoking, history of late miscarriage or preterm delivery and Afro–Carribbean origin (Robinson & Norwitz, 2005). In twin pregnancies the risk for preterm rupture of membranes is doubled in twin pregnancies compared to singleton pregnancies (Myles et al., 1997). Pregnancy complications like preeclampsia, hypertension and growth restriction which are associated with preterm delivery occur more often in twin pregnancies than in singleton pregnancies (Savvidou et al., 2001; Sebire et al., 1997). Additional mechanism for preterm births in multiple gestations may be related to the different endocrine environment in multiple pregnancies (Robinson & Norwitz, 2005). Progesterone, estrogen and sex steroids are proportionally increased in twin pregnancies compared to singleton pregnancies. Increased steroid production may play a role in initiation of preterm delivery in twin pregnancies. In particular, higher circulating levels of relaxin are associated with

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super-ovulation and may cause preterm delivery (Iams et al., 2001). Interestingly, no correlation was observed between high relaxin levels and shortening of the cervix (Iams et al., 2001).

Most spontaneous preterm deliveries occur in women without a risk factor in their history. Measurement of cervical length and testing for fetal fibronectin in cervico-vaginal secretions improve prediction of preterm delivery in singleton pregnancies (Leitich, 2005). A recent study on 1200 twins showed that cervical length is also an independent predictor for spontaneous preterm delivery in twins (To et al., 2006).

Our aim was to evaluate the association of cervical length at 20–25 weeks of gestation on spontaneous delivery before 34 weeks in twin pregnancies in a country with a high incidence of preterm delivery compared to other European countries.

Materials and Methods

Patients

Routine antenatal care in twin pregnancies at the Department of Obstetrics and Feto-Maternal Medicine of the Medical University Vienna includes measurement of the cervical length at 20 to 25 weeks of gestation. Over a period of 3 years, 262 consecutive patients with twin pregnancies older than 18 years had a scan of the cervical length. Women who were symptomatic at 20 to 25 weeks (uterine contractions or vaginal bleeding) and who delivered because of other reasons than spontaneous labour and preterm rupture of membranes or at term were excluded. Measurements of the cervical length were performed by one of five well-trained operators. The patients were examined in the supine position with flexed hips and knees. After emptying the bladder the ultrasound probe was placed within the introitus vaginae and moved forward to the anterior fornix of the vagina. Pressure on the cervix was avoided during the measurement. When the internal and the external os were clearly visible and the whole length of the cervical canal with an echogenic endocervical mucosa was obtained, cervical length was measured and recorded.

Two hundred and sixty-two consecutive patients with twin pregnancies had a scan of the cervical length at 20–25 weeks of gestation. After exclusion of 39 women (Table 1), the study cohort consisted of 223 patients.

Cervical length at 20–25 weeks of gestation, previous preterm delivery before 34 weeks of gestation, chorionicity, maternal age, body-mass-index, smoking habit and parity were recorded as risk factors for preterm delivery. Patient characteristics of the study population are shown in Table 2.

Statistical Analyses

Statistical analyses were performed with SPSS software (version 12.0; SPSS, Chicago, IL). Parametric continuous variables are summarized as means (± standard deviation), non parametric continuous variables are summarized as medians (minimum and maximum) and categorical data as percentages. The Fisher's exact test was used for comparisons of gestational age at birth in women with a cervical length under 25 mm and more than 25 mm, under 30 mm and more than 30 mm and under 35 mm and more than 35 mm at 20–25 weeks of gestation. Logistic regression analysis was used to identify independent predictors of preterm delivery before 34 weeks of gestation. Independent variables entered into the regression models were cervical length at 20 to 25 weeks of gestation, parity, chorionicity, maternal age and body-mass-index and smoking habit. Effects are reported as odds ratios (ORs) and 95% confidence intervals (CI). *P* values of $< .05$ were considered significant.

Table 1

Excluded Patients

	% (*n*)
Contractions at 20–25 weeks	2.7 (7/262)
Vaginal bleeding at 20–25 weeks	0.4 (1/262)
Delivery because of preeclampsia	0.4 (1/262)
Delivery because of HELLP	0.4 (1/262)
Delivery because of growth restriction	2.0 (5/262)
Delivery because of threatening fetal asphyxia	8 (21/262)
Delivery because of fetal malformation	0.4 (1/262)
Delivery because of suspected abruption of placenta	0.8 (2/262)

Table 2

Patient Characteristics of the Study Population

Maternal age (y [mean ± *SD*])	31.1 ± 5.48
Body-mass-index (kg/m²) [median, range]	23.0 (16.8;42.3)
Smoking (%, *n*)	16.1 (36/223)
Primiparae (%, *n*)	55.6 (124/223)
Multiparae (%, *n*)	44.4 (99/223)
Dichorionic twins (%, *n*)	82.9 (185/223)
Monochrionic twins (%, *n*)	17.0 (38/223)
Previous preterm delivery before 37 weeks of gestation (%, *n*)	4.5 (10/223)
Previous preterm delivery before 34 weeks of gestation (%, *n*)	2.2 (5/223)

Results

Cervical length at 20–25 weeks of gestation was normally distributed (Figure 1). The median of the cervical length was 36 mm (range: 7–74 mm). The median gestational age at birth was 36.1 weeks of gestation (range 25.1–39.1 weeks). Six women (2.7%) delivered before 28 weeks of gestation, 12 (5.4%) delivered before 30 weeks of gestation, 20 (9%) before 32 weeks of gestation and 32 (14.3%) before 34 weeks of gestation.

There were 10 women (5%) with cervical length less than 25 mm. A correlation between cervical length lower than 25 mm and spontaneous delivery

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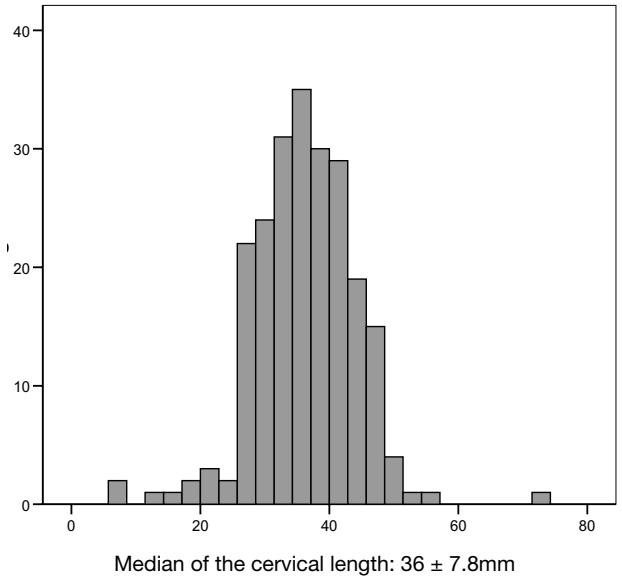

Figure 1

Distribution of the cervical length at 20-25 weeks of gestation.

before 34 weeks (50% vs. 13%, p = .007) was found (Figure 2). There was also a correlation between cervical length of less than 30 mm and less than 35 mm and spontaneous delivery before 34 weeks (29% vs. 11%, p = .005, 26.1% vs. 6.7%, p < .001). In addition, logistic regression analysis found cervical length to be the only independent significant predictor of spontaneous delivery before 34 weeks. (OR 1.084; 95 % CI 1.015; 1.159; p = .017).

Previous preterm delivery, chorionicity, maternal age, body-mass-index, smoking habit and parity were not statistically significant in the logistic regression model (Table 3). Figure 3 shows examples for a short cervical length and for a normal cervical length.

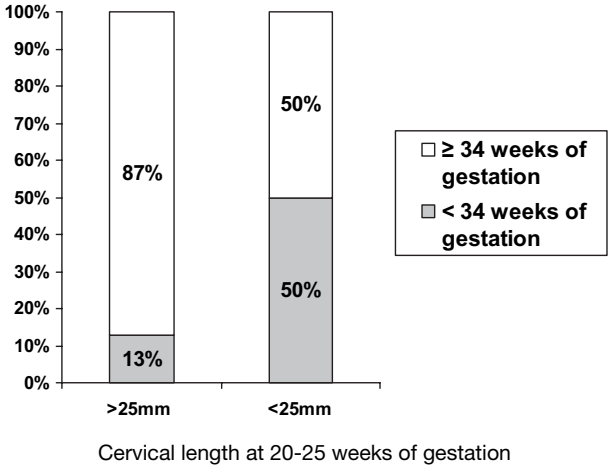

Figure 2

Cervical length at 20-25 weeks of gestation and preterm delivery before 34 weeks of gestation.

Table 3

Logistic Regression Model

Risk factors	Odds ratio	95% CI	p value
Cervical length	1.084	1.015–1.159	.017
Previous preterm delivery	4.947	0.411–59.602	.208
Chorionicity	0.726	0.237–2.224	.575
Maternal age	1.08	0.986–1.184	.098
Body-mass-index	1.053	0.924–1.201	.438
Smoking	0.768	0.212–2.778	.687
Parity	1.784	0.836–3.69	.118

Discussion

This study has demonstrated that the rate of spontaneous delivery before 34 weeks of gestation in women with twin pregnancies is predictable from measurement of cervical length at 20–25 weeks of gestation in a country with a high incidence of preterm delivery compared to other European countries. Cervical length measurements smaller than 35 mm, 30 mm and 25 mm at 20–25 weeks of gestation are associated with a higher risk for spontaneous delivery before 34 weeks of gestation in twin pregnancies compared to greater measurements. Regression analysis identified the cervical length as the only independent significant predictor for spontaneous delivery before 34 weeks.

The association between cervical shortening and preterm delivery has been described before. Odibo et al. (2001) observed in a population of singleton pregnancies with a high risk for preterm birth that the progressive shortening of the cervix to 10 mm or less or cervical funnelling of more than 75% was predictive for preterm premature rupture of membranes (Odibo et al., 2001). According to a review from 2002, trials investigating the usefulness and correct gestation for cervical screening in multiple gestations are required as cervical screening is worse defined than in singletons and there are significantly less published trials (Welsh & Nicolaides, 2002). In several previous studies, the median cervical length does not differ between singleton and twin pregnancies, but the rate of cervical lengths ≤ 25 mm is higher in twin pregnancies (12.9% versus 8.4%), that is consistent with the higher rate of preterm delivery in twin pregnancies (Odibo et al., 2001; Williams & Iams, 2004).

Similar to our data, the Preterm Prediction Study confirmed a relationship between cervical length measured at 24 and 28 weeks of gestation and preterm birth in twin pregnancies (Iams et al., 2001). Furthermore, Skentou et al. examined 464 twin pregnancies and showed an inverse correlation between cervical length and the rate of delivery before 33 weeks of gestation (Skentou et al., 2001). Eight per cent of the patients had a cervix shorter than 20 mm; their risk for delivery before 33 weeks of gestation was 17%. We could observe an increase in risk for preterm delivery before 34 weeks to 50% using 25

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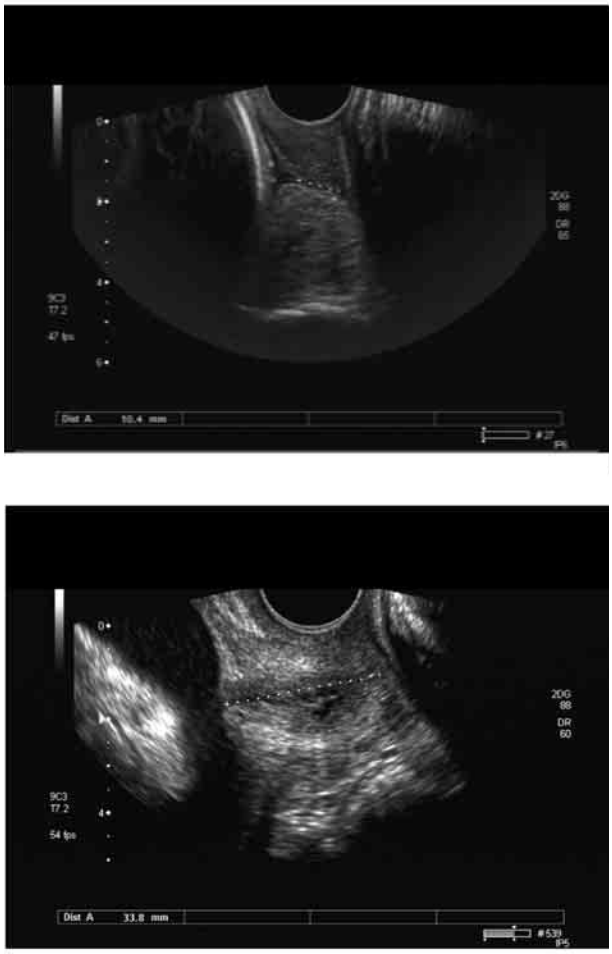

Figure 3

Examples for a short cervical length and for a normal cervical length.

mm as cut-off in our population. For the same cut-off, Souka et al. described that of 45% delivered before 32 weeks of gestation (Souka et al., 1999). Yang et al. examined 65 twin pregnancies using translabial or transvaginal ultrasonography. They observed that a cervical length of 30 mm or less and cervical funnelling before 26 weeks were independently associated with preterm birth before 32 weeks (Yang et al., 2000). Only one study concluded that cervical length measurements were not predictive for preterm birth before 35 weeks of gestation (Ong et al., 2000).

Summarizing experimental and clinical evidence, not all reasons for preterm delivery are associated with shortening of the cervix. Some preterm deliveries result from pathologic distention of the uterus, decidual-chorioamniotic or systemic inflammation, activation of the maternal or fetal hypothalamic-pituitary-adrenal axis and decidual hemorrhage. Hence, using the cervical length for predicting preterm delivery has some limitations. However, different reasons for spontaneous preterm delivery result in a final common pathway leading to myometrial activation and cervical dilatation (Lockwood & Kuczynski, 1999).

There are several trials on prevention of preterm delivery by cervical cerclage in twin pregnancies with short cervix with controversial results. (Althusius et al., 2001; Berghella et al., 2004; Rust et al., 2001; To et al., 2004). A meta-analysis concluded that in singleton pregnancies with a short cervical length, especially those who had previously delivered preterm or with a prior late miscarriage, the rate of preterm delivery was reduced when cerclage was performed. In contrast, in twin pregnancies cerclage was associated with an increased risk of preterm delivery (Berghella et al., 2005).

Until today no prophylactic treatment has been established to decrease the rate of preterm births in twin pregnancies. There are small trials assessing infections (McMahon et al., 2002), and no data on antibiotic treatment for prevention of preterm birth in twins. A recent meta-analysis concluded that antibiotic treatment does not reduce the risk of preterm birth in singleton pregnancies at risk (Simcox et al., 2007).

Progesterone was ineffective as compared with placebo in reducing the rate of delivery before 35 weeks in twin pregnancies in a recently published randomised trial (Rouse et al., 2007). In contrast, trials investigating singleton pregnancies at high risk of preterm birth presented a significant decrease of the rate of preterm delivery under prophylactic treatment with progesterone (da Fonseca et al., 2003; da Fonseca et al., 2007; Meis et al., 2003). However, they have failed to show an improvement in fetal outcome.

Our results demonstrate that measurement of the cervical length at 20 to 25 weeks of gestation can predict the prevalence of preterm delivery before 34 weeks of gestation in twin pregnancies. The overall rate of preterm delivery in twins is high; therefore, research on the prevention of preterm birth should include all twin pregnancies, irrespective of cervical length.

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