ORIGINAL ARTICLE

Cervical Length at Mid-Pregnancy and the Risk of Primary Cesarean Delivery

Gordon C.S. Smith, M.D., Ph.D., Ebru Celik, M.B., Ch.B., Meekai To, M.B., Ch.B., Olga Khouri, M.B., Ch.B., and Kypros H. Nicolaides, M.D., for the Fetal Medicine Foundation Second Trimester Screening Group

ABSTRACT

BACKGROUND

Physiological and biochemical studies suggest that normal parturition at term is dependent on programmed development of the uterus in early pregnancy. It is recognized that a short cervix in mid-pregnancy is associated with an increased risk of spontaneous preterm birth. We hypothesized that a long cervix in mid-pregnancy would be associated with an increased risk of cesarean delivery during labor at term.

METHODS

We studied 27,472 primiparous women who had a cervical length of 16 mm or more at a median of 23 weeks of gestation and who ultimately delivered a live infant in labor at term.

RESULTS

The rate of cesarean delivery at term was lowest (16.0%) among women with a mid-pregnancy cervical length in the lowest quartile (16 to 30 mm) and was significantly greater in the second quartile (18.4%, 31 to 35 mm), third quartile (21.7%, 36 to 39 mm), and fourth quartile (25.7%, 40 to 67 mm) (P<0.001 for trend). The odds ratio for cesarean delivery among women in the fourth quartile, as compared with the first quartile, was 1.81 (95% confidence interval [CI], 1.66 to 1.97), and the odds ratio adjusted for maternal age, body-mass index, smoking status, race or ethnic group, gestational age at birth, spontaneous or induced labor, birth-weight percentile, and hospital of delivery was 1.68 (95% CI, 1.53 to 1.84; P<0.001). The increased risk of cesarean delivery was attributable to procedures performed for poor progress in labor.

CONCLUSIONS

The cervical length at mid-pregnancy is an independent predictor of the risk of cesarean delivery at term in primiparous women.

From the Department of Obstetrics and Gynaecology, Cambridge University, Cambridge, United Kingdom (G.C.S.S.); and the Harris Birthright Research Centre for Fetal Medicine, King's College Hospital Medical School, London (E.C., M.T., O.K., K.H.N.). Address reprint requests to Dr. Smith at the Department of Obstetrics and Gynaecology, Cambridge University, Box 223, Rosie Maternity Hospital, Cambridge CB2 2SW, United Kingdom, or at gcss2@cam.ac.uk.

N Engl J Med 2008;358:1346-53.

Rates of cesarean delivery have increased dramatically throughout the developed world in recent years.[1] This trend has recently increased because of declining rates of vaginal birth after cesarean delivery.[1] With the decrease in vaginal birth after cesarean delivery, the rate of primary cesarean delivery will become an even more important determinant of overall cesarean rates. The major cause of primary cesarean delivery is poor progress during labor (dystocia).[2] A number of risk factors for such poor progress have been identified, such as advanced maternal age,[3] obesity,[4] and delivery after 40 weeks of gestation.[5] However, the biologic mechanisms that lead to poor progress during labor are poorly understood.

Studies of parturition in animals suggest that preparation for labor is evident at relatively early stages of gestation.[6,7] In women, it is well recognized that the cervix undergoes preparative changes in the weeks before the onset of labor[8] and also that a short cervix in mid-pregnancy is associated with an increased risk of spontaneous preterm birth.[9] We conducted a study to determine whether the length of the cervix in mid-pregnancy was associated with the risk of intrapartum cesarean delivery at term among primiparous women.

METHODS

The data analyzed in our study were obtained as part of multicenter studies of screening and intervention during pregnancy, conducted between 1998 and 2006, at eight hospitals in and around London: Basildon Hospital, Basildon; Queen Elizabeth Hospital, Woolwich; Harold Wood Hospital, Romford; King George Hospital, Ilford; King's College Hospital, London; Queen Mary's Hospital, Sidcup; University Hospital, Lewisham, London; and Southend University Hospital, Essex. Women recruited to the studies underwent transvaginal ultrasonography, including assessment of cervical length and uterine-artery Doppler flow velocimetry, between 22 and 24 weeks of gestation. Women with a short cervix (15 mm or less in length) recruited between January 1998 and May 2002 were offered participation in a trial of cervical cerclage, and those recruited between September 2003 and May 2006 were offered participation in a trial of vaginal administration of progesterone. Between January 2001 and July 2002, women with a mean pulsatility index of 1.6 or more (representing approximately the top 5% of values in the general population, with increasing values indicating decreasing diastolic velocity, a measure of placental impedance to blood flow) were offered participation in a trial of low-dose aspirin as prophylaxis for preeclampsia. The details of these trials are reported elsewhere.[10-12]

Measurements of cervical length were performed with the use of transvaginal ultrasonographic images[13] by ultrasonographers trained in these methods. Quality control of the screening, handling of data, and verification of adherence to protocols at the various centers was performed on a regular basis by the trial coordinators. Clinical details and medical and obstetrical histories were obtained during face-to-face interviews with the mothers that were conducted by a research obstetrician using a structured questionnaire.

The inclusion criteria for the current analysis were that the women were primiparous, had a cervical-length measurement performed, and ultimately delivered at term. We excluded women who had a stillbirth or therapeutic abortion, women whose cervical length was 15 mm or less, and women whose infants were delivered by prelabor cesarean section. Hence, all women randomly assigned to either the control group or the interventional group of the cervical-cerclage trial or the progesterone trial were excluded from the present study.

The outcome of each pregnancy was obtained from the computerized delivery records in each participating hospital. This information included data on the mode of delivery, the gestational age at birth, whether the patient was in labor, whether the onset of labor was spontaneous or induced, and the indications for operative delivery. Outcome data for the infant were also recorded, including whether the birth was a live birth or stillbirth, the birth weight, and the sex. The data were entered into the computer soon after delivery by the attending midwife or obstetrician. The primary outcome was cesarean delivery performed during labor at term. We performed subgroup analyses on the basis of whether the indication or indications for cesarean delivery recorded in the computerized medical records included a failure to progress in labor.

These studies were approved by the South

Thames Multicenter Research Ethics Committee, as well as the local ethics committees of the individual hospitals. Written informed consent was obtained from the women who agreed to participate.

STATISTICAL ANALYSIS

Continuous variables were summarized by calculating the median and interquartile range, and subgroups of patients were compared with the use of the Kruskal–Wallis test. Univariate comparisons of categorical data were performed with the chi-square test for trend. All reported P values are two-sided, and a P value of less than 0.05 was considered to indicate statistical significance. Birth weight was analyzed as the percentile for sex and week of gestation. For the analysis of main effects, all variables were categorized. Adjusted odds ratios were obtained by means of multivariable logistic-regression analysis.[14] The independent variables included were cervical length, maternal age, body-mass index, smoking status, race or ethnic group, gestational age at birth, spontaneous or induced labor, birth-weight percentile, and hospital of delivery.

We planned to assess the interaction between cervical length and all other variables. We tested interaction terms between cervical length and other maternal variables using cervical length as a continuous variable and the other variables as categorical variables. The statistical significance of the interactions was assessed with the use of backward stepwise regression, in which statistical significance was estimated by means of the likelihood-ratio test to assess the effect of removing interaction terms for all strata of the given variable.[14] Given that eight tests of interaction were performed, the threshold for statistical significance for interaction terms was reduced to P values of less than 0.00625 (according to the Bonferroni method). Since cesarean delivery is a common outcome, adjusted odds ratios from multivariable logistic regression were converted into adjusted relative risks, according to the method of Zhang and Yu.[15] Adjusted relative risks were compared with adjusted incidence-rate ratios obtained from Poisson regression.[16] We estimated attributable fractions by using the method of Greenland and Drescher.[17] All statistical analyses were performed with the Stata software package, version 10.

RESULTS

Data were available from a total of 59,314 women. We excluded 682 records (1.1%) because the patient had a cervical length of 15 mm or less and 252 records (0.4%) because of a stillbirth or therapeutic abortion. A total of 58,405 women (98.5%) had neither outcome, and 30,452 of these women (52.1%) were primiparous. Of these 30,452 women, 1635 (5.4%) delivered preterm; of the remaining 28,817 women, 1345 (4.7%) delivered by prelabor cesarean section. This left a study group of 27,472 women, representing 90.2% of all eligible primiparous women screened. The median gestational age at the time of measurement of cervical length was 23 weeks (interquartile range, 22 weeks 5 days to 23 weeks 2 days).

Table 1 summarizes the characteristics of the cohort in relation to the quartile of cervical length. The cervical length at 23 weeks of gestation was positively associated with increasing maternal age, nonsmoking (vs. smoking), increasing body-mass index, white race, increasing gestational age at birth, induced (vs. spontaneous) labor, and increasing birth-weight percentile. A total of 5542 women underwent cesarean section. In 4615 of these procedures (83.3%), failure of labor to progress was included in the list of indications.

The rate of cesarean delivery was lowest among women with a cervical length at 23 weeks in the lowest quartile (16.0%) and was significantly greater in the second quartile (18.4%), third quartile (21.7%), and fourth quartile (25.7%) (P<0.001 for trend). The risk of cesarean delivery increased with increasing absolute values of midpregnancy cervical length. Rates of cesarean delivery started to rise at a cervical length of 25 mm and plateaued at a cervical length of 50 mm, approximately doubling across the range of observed values (Fig. 1). The association between cervical length and the rate of cesarean delivery was attributable to the procedure being performed in women for whom the indication included poor progress during labor.

Adjustment for a range of characteristics (maternal age, body-mass index, smoking status, race or ethnic group, gestational age at birth, spontaneous or induced labor, birth-weight percentile, and hospital of delivery) slightly attenuated but did not eliminate the significant association bet-

Table 1. Baseline Characteristics of the Cohort, According to the Quartile of Cervical Length at 23 Weeks of Gestation.*

Maternal Characteristic or Outcome	Quartile of Cervical Length				P Value
	1 (N=7061)	2 (N=8075)	3 (N=6065)	4 (N=6271)	
Cervical length — mm	16–30	31–35	36–39	40–67	<0.001
Age — yr					
Median	27.0	28.0	28.8	29.4	<0.001
IQR	22.0–31.5	23.0–31.7	24.2–32.0	25.3–32.9	
Body-mass index†					
Median	23.5	23.8	23.9	24.2	<0.001
IQR	21.3–26.5	21.5–26.7	21.6–27.0	22.0–27.3	
Current smoker — no. (%)	949 (13.4)	1027 (12.7)	685 (11.3)	586 (9.3)	<0.001
Race or ethnic group — no. (%)‡					
White	4384 (62.1)	5653 (70.0)	4483 (73.9)	4726 (75.4)	<0.001
Black	1963 (27.8)	1592 (19.7)	1054 (17.4)	1046 (16.7)	<0.001
Other	714 (10.1)	830 (10.3)	528 (8.7)	499 (8.0)	<0.001
Gestational age at birth — wk					
Median	40.0	40.0	40.0	40.3	<0.001
IQR	39.0–41.0	39.0–41.0	39.1–41.0	39.4–41.1	
Induced labor — no. (%)	1101 (15.6)	1444 (17.9)	1068 (17.6)	1402 (22.4)	<0.001
Birth-weight percentile					
Median	46	49	52	54	<0.001
IQR	21–72	25–74	28–76	28–78	
Cesarean delivery — no. (%)					
All	1133 (16.0)	1482 (18.4)	1315 (21.7)	1612 (25.7)	<0.001
Poor progress during labor§	884 (12.5)	1195 (14.8)	1101 (18.2)	1435 (22.9)	<0.001
Other	249 (3.5)	287 (3.6)	214 (3.5)	177 (2.8)	0.03

* Numbers among the quartiles are unequal owing to ties. P values were calculated with the use of the chi-square test for trend or the Kruskal–Wallis test, as appropriate. IQR denotes interquartile range.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Race or ethnic group was self-reported.
§ Poor progress during labor was reported in computerized medical records listing this condition as an indication for cesarean delivery.

tween cervical length and the risk of cesarean delivery at term (Table 2). When the outcome was limited to cesarean delivery because of a failure of labor to progress, the association with cervical length was slightly stronger (see the Supplementary Appendix, available with the full text of this article at www.nejm.org). There were no significant interactions between cervical length and any of the maternal characteristics in predicting the risk of intrapartum cesarean delivery (Fig. 2). The interaction between cervical length and birth-weight percentile had a P value of 0.01, but this value was greater than 0.00625, the threshold of significance used for the analysis of interaction, and the stratified analysis showed no clear pattern of interaction across the strata of birth-weight percentile (Fig. 2).

The attributable fraction for cesarean delivery associated with the upper three quartiles of cervical length was 20.5% (95% confidence interval [CI], 16.6 to 24.1). After adjustment for maternal characteristics, this fraction was 17.2% (95% CI, 13.4 to 20.9).

Since cesarean delivery was common, the output of logistic-regression models was also expressed as the adjusted relative risk.[15] The ad-

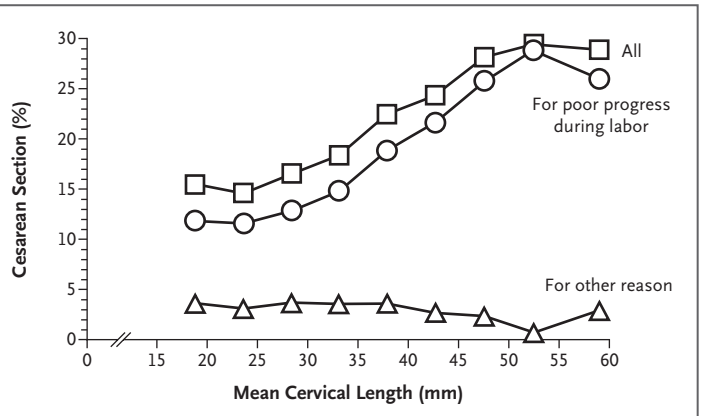

Figure 1. Proportion of Cesarean Deliveries in Relation to Absolute Values of Cervical Length Measured at 23 Weeks of Gestation.

justed relative risk of cesarean delivery for the highest quartile of cervical length was 1.49 (95% CI, 1.39 to 1.59). This value was very similar to the adjusted incidence-rate ratio (1.45; 95% CI, 1.34 to 1.57) estimated with the use of Poisson regression, an analysis that is also recommended for common outcomes.[16]

DISCUSSION

We found that the risk of intrapartum cesarean delivery at term among primiparous women was associated with the length of the cervix in mid-pregnancy. The risk of cesarean delivery began to increase when the cervical length at 23 weeks was greater than 25 mm and approximately doubled across the range of lengths. The relationship persisted after adjustment for several maternal characteristics. There was no strong evidence of an interaction between cervical length and other factors associated with the risk of cesarean delivery. These findings suggest that cervical length at mid-pregnancy is an important indicator of the risk of primary cesarean delivery at term.

We hypothesize that poor progress during labor at term is determined by the development of the uterus at much earlier stages of pregnancy. In the present study, we tested a prediction arising from that hypothesis — namely, that a long cervix in mid-pregnancy would be associated with an increased risk of emergency cesarean delivery during labor at term. The most common cause of intrapartum primary cesarean section is poor progress during labor. This is cited as the sole indication, or as a joint indication with fetal distress, in approximately 80% of intrapartum procedures at term among primiparous women,[18] and the proportion was very similar in the present study. Our analysis of cesarean delivery according to the indication for it was consistent with this finding, showing that the increased risk of this event among women who had a long cervix in mid-pregnancy was explained by the increased risk of poor progress during labor. It has previously been shown that cervical length at 37 weeks of gestation is strongly associated with the risk of cesarean section for poor progress during labor.[19] Our study did not involve serial measurement of cervical length throughout pregnancy. Hence, we could not determine whether the association between cervical length at mid-pregnancy and the risk of cesarean delivery at term was related to the cervical length at earlier or later gestational ages.

Our findings are consistent with those from studies of a range of animal species, which have shown that changes in preparation for labor and delivery occur through the second half of pregnancy,[8] and from longitudinal studies of pregnant rodents, which have showed a clear pattern of biochemical changes occurring in mid-pregnancy that are preparative for the ultimate process of labor.[7,20] The relation between such physiological and biochemical changes in mid-pregnancy in animals and variation in the cervical length at mid-pregnancy in women is currently unclear. Further study is needed to assess the possibility that a long cervix in mid-pregnancy may reflect dysfunctional development of the uterus, which is ultimately manifested in the need for cesarean delivery at term.

This study was a secondary analysis of data that were obtained for other purposes. Because the primary outcome of the original interventional trials was spontaneous preterm birth, the indication for cesarean delivery was ascertained only from the computerized delivery record, and we do not have data to validate the listed indications. Moreover, it is possible that the association between cervical length at mid-pregnancy and the risk of cesarean delivery was a chance finding. However, the association was signifi-

Table 2. Unadjusted and Adjusted Odds Ratios for Cesarean Delivery, According to Overall Outcome Characteristics.

Variable	Unadjusted Analysis		Adjusted Analysis	
	Odds Ratio (95% CI)	P Value	Odds Ratio (95% CI)*	P Value
Quartile of cervical length				
1 (referent)	1.0		1.0	
2	1.18 (1.08–1.28)	<0.001	1.16 (1.06–1.27)	0.001
3	1.45 (1.33–1.58)	<0.001	1.43 (1.31–1.57)	<0.001
4	1.81 (1.66–1.97)	<0.001	1.68 (1.53–1.84)	<0.001
Age				
<20 yr	0.44 (0.39–0.51)	<0.001	0.49 (0.42–0.56)	<0.001
20–24 yr	0.67 (0.61–0.73)	<0.001	0.69 (0.62–0.76)	<0.001
25–29 yr (referent)	1.0		1.0	
30–34 yr	1.19 (1.11–1.29)	<0.001	1.23 (1.14–1.33)	<0.001
35–39 yr	1.57 (1.42–1.73)	<0.001	1.57 (1.41–1.74)	<0.001
≥40 yr	1.71 (1.37–2.15)	<0.001	1.59 (1.25–2.03)	<0.001
Body-mass index (before pregnancy)				
<20.0	0.72 (0.63–0.81)	<0.001	0.82 (0.73–0.93)	<0.001
20.0–24.9 (referent)	1.0		1.0	
25.0–29.9	1.57 (1.47–1.68)	<0.001	1.40 (1.30–1.50)	<0.001
30.0–34.9	2.02 (1.83–2.24)	<0.001	1.68 (1.51–1.87)	<0.001
≥35.0	2.60 (2.27–2.97)	<0.001	2.05 (1.77–2.37)	<0.001
Current smoker				
No (referent)	1.0		1.0	
Yes	0.73 (0.66–0.81)	<0.001	1.04 (0.94–1.16)	0.45
Race or ethnic group				
White (referent)	1.0		1.0	
Black	1.40 (1.30–1.50)	<0.001	1.81 (1.66–1.97)	<0.001
Other	0.96 (0.86–1.06)	0.40	1.41 (1.26–1.59)	<0.001
Gestational age at birth				
37 wk	1.20 (1.05–1.38)	0.009	1.01 (0.87–1.17)	0.87
38 wk	0.88 (0.79–0.98)	0.02	0.78 (0.70–0.88)	<0.001
39 wk	0.78 (0.71–0.85)	<0.001	0.75 (0.68–0.82)	<0.001
40 wk (referent)	1.0		1.0	
41 wk	1.47 (1.36–1.59)	<0.001	1.25 (1.15–1.36)	<0.001
≥42 wk	2.38 (2.13–2.67)	<0.001	1.44 (1.27–1.64)	<0.001
Onset of labor				
Spontaneous (referent)	1.0		1.0	
Induced	2.80 (2.61–2.99)	<0.001	2.37 (2.19–2.56)	<0.001
Birth-weight percentile				
1–3	1.51 (1.29–1.77)	<0.001	1.49 (1.26–1.77)	<0.001
4–10	0.92 (0.81–1.04)	0.16	0.91 (0.80–1.03)	0.15
11–20	0.83 (0.75–0.93)	0.001	0.85 (0.76–0.96)	0.007
21–80 (referent)	1.0		1.0	
81–90	1.40 (1.27–1.54)	<0.001	1.35 (1.22–1.49)	<0.001
91–97	1.85 (1.67–2.06)	<0.001	1.81 (1.62–2.03)	<0.001
98–100	3.15 (2.73–3.65)	<0.001	2.87 (2.46–3.36)	<0.001

* These odds ratios and 95% CIs were adjusted for maternal age, body-mass index, smoking status, race or ethnic group, gestational age at birth, spontaneous or induced labor, birth-weight percentile, and hospital of delivery.

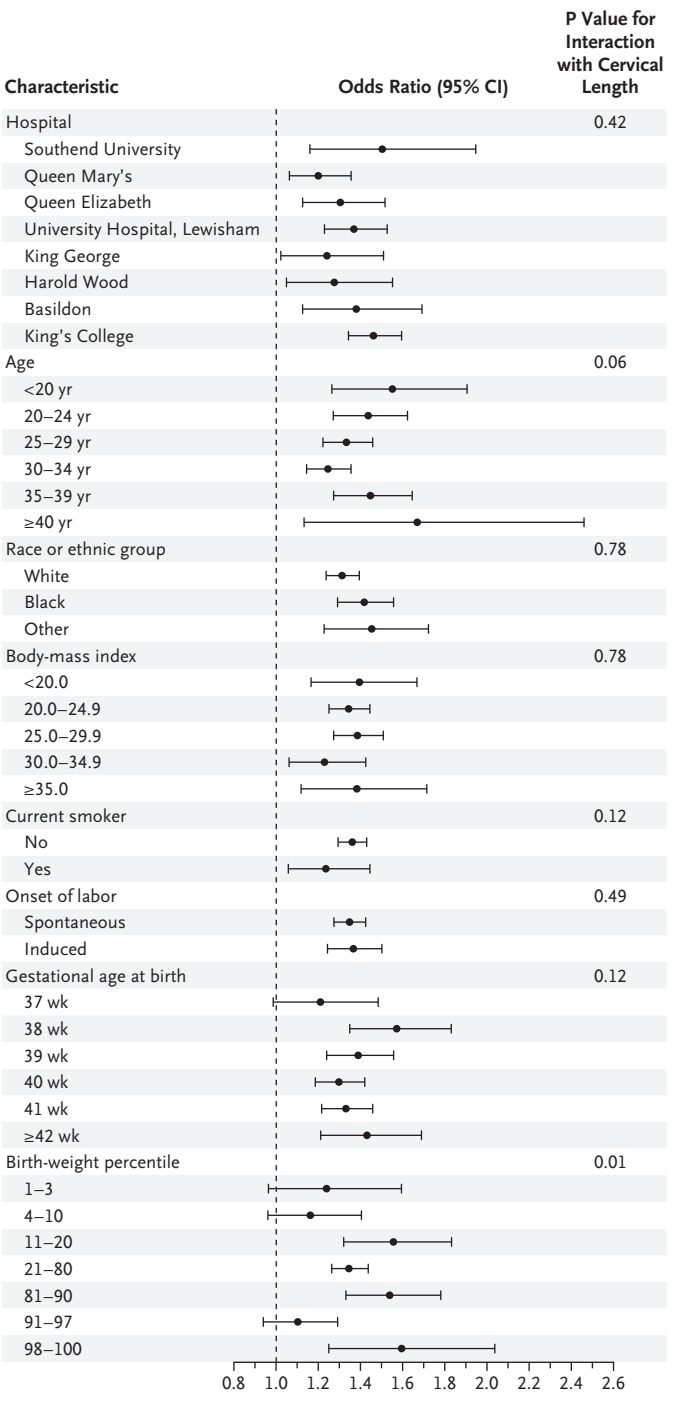

Figure 2. Odds Ratios for Cesarean Delivery per 10-mm Increase in Cervical Length, According to Overall Outcome Characteristics.

Odds ratios were stratified for each characteristic and adjusted for all other characteristics listed. P values were estimated with the use of the likelihood-ratio test. Given that eight comparisons were made, the threshold for statistical significance was P<0.00625.

cant at a P value of less than 0.001. Hence, the probability of this being a chance finding is very low. Although the association persisted in the multivariable analysis, it is also possible that it reflects residual confounding either due to a failure to measure important maternal variables directly or due to unmeasured confounders. For example, body-mass index is a proxy measure of adiposity, and residual confounding by this variable cannot be ruled out. If residual confounding by obesity explained the association found in the multivariable analysis, it is likely that an interaction between body-mass index and cervical length would have been observed. However, the association between cervical length and emergency cesarean delivery was similar among lean women, those of normal weight, and those who were overweight or obese (Fig. 2). Similarly, the relation between cervical length and cesarean delivery was consistent across strata of other maternal and outcome factors and across the eight hospitals studied.

Our study excluded women who delivered preterm. Women who deliver preterm are a heterogeneous group, consisting both of those with spontaneous preterm births and those with indicated preterm births. Moreover, intrapartum cesarean delivery for breech presentation is common before term, and the inclusion of preterm births would have complicated the interpretation of associations between cervical length and cesarean delivery for failure of labor to progress. Since the study group consisted of approximately 90% of all primiparous women screened, our findings are relevant to the general population of primiparous women.

Poor progress during labor at term is the most common indication for primary cesarean section and, hence, an important determinant of overall rates of cesarean section. Our finding that a long cervix in mid-pregnancy is predictive of cesarean section during labor at term suggests that poor progress during labor in women who deliver at term may be related to dysfunctional development of the uterus at much earlier stages of pregnancy.

Supported by a grant from the Fetal Medicine Foundation (1037116).

No potential conflict of interest relevant to this article was reported.

APPENDIX

The members of the Fetal Medicine Foundation Second Trimester Screening Group were as follows: *University Hospital Lewisham, London:* A. Delfino, M. Fokialaki, S. Flint; *Queen Elizabeth Hospital, Woolrich:* F. Molina, S. Turan, K. Gajewska, V. Palanappian; *King's College Hospital, London:* E. Karanastasi, A.M. Cacho, C. Skentou; *King George Hospital, Ilford:* L. Thompson, J. Webber, E. Osei; *Basildon Hospital, Basildon:* M.S. To, G. Fletcher, J. Parminter; *Harold Wood Hospital, Romford:* A. Moakes, C. Otigbah, R. Utidjian; *Queen Mary's Hospital, Sidcup:* S. Preston, A. Morgan, A. Abbas; *Southend University Hospital, Essex:* P. Hagan, M. Singh — all in the United Kingdom.

REFERENCES

1. Ecker JL, Frigoletto FD Jr. Cesarean delivery and the risk-benefit calculus. N Engl J Med 2007;356:885-8.

2. Macara LM, Murphy KW. The contribution of dystocia to the cesarean section rate. Am J Obstet Gynecol 1994;171:71-7.

3. Main DM, Main EK, Moore DH II. The relationship between maternal age and uterine dysfunction: a continuous effect throughout reproductive life. Am J Obstet Gynecol 2000;182:1312-20.

4. Crane SS, Wojtowycz MA, Dye TD, Aubry RH, Artal R. Association between pre-pregnancy obesity and the risk of cesarean delivery. Obstet Gynecol 1997;89:213-6.

5. Smith GCS, White IR, Pell JP, Dobbie R. Predicting cesarean section and uterine rupture among women attempting vaginal birth after prior cesarean section. PLoS Med 2005;2(9):e252.

6. Figueroa JP, Mahan S, Poore ER, Nathanielsz PW. Characteristics and analysis of uterine electromyographic activity in the pregnant sheep. Am J Obstet Gynecol 1985;151:524-31.

7. Shynlova O, Oldenhof A, Dorogin A, et al. Myometrial apoptosis: activation of the caspase cascade in the pregnant rat myometrium at midgestation. Biol Reprod 2006;74:839-49.

8. Garfield RE, Saade G, Buhimschi C, et al. Control and assessment of the uterus and cervix during pregnancy and labour. Hum Reprod Update 1998;4:673-95.

9. Iams JD, Goldenberg RL, Meis PJ, et al. The length of the cervix and the risk of spontaneous premature delivery. N Engl J Med 1996;334:567-72.

10. Yu CK, Papageorghiou AT, Parra M, Palma Dias R, Nicolaides KH. Randomized controlled trial using low-dose aspirin in the prevention of pre-eclampsia in women with abnormal uterine artery Doppler at 23 weeks' gestation. Ultrasound Obstet Gynecol 2003;22:233-9.

11. To MS, Alfirevic Z, Heath VC, et al. Cervical cerclage for prevention of preterm delivery in women with short cervix: randomised controlled trial. Lancet 2004;363:1849-53.

12. Fonseca EB, Celik E, Parra M, Singh M, Nicolaides KH. Progesterone and the risk of preterm birth among women with a short cervix. N Engl J Med 2007;357:462-9.

13. Albaiges G, Missfelder-Lobos H, Lees C, Parra M, Nicolaides KH. One-stage screening for pregnancy complications by color Doppler assessment of the uterine arteries at 23 weeks' gestation. Obstet Gynecol 2000;96:559-64.

14. Hosmer DW, Lemeshow S. Applied logistic regression. 2nd ed. New York: John Wiley, 2000.

15. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA 1998;280:1690-1.

16. Greenland S. Model-based estimation of relative risks and other epidemiologic measures in studies of common outcomes and in case-control studies. Am J Epidemiol 2004;160:301-5.

17. Greenland S, Drescher K. Maximum likelihood estimation of the attributable fraction from logistic models. Biometrics 1993;49:865-72.

18. Ecker JL, Chen KT, Cohen AP, Riley LE, Lieberman ES. Increased risk of cesarean delivery with advancing maternal age: indications and associated factors in nulliparous women. Am J Obstet Gynecol 2001;185:883-7.

19. Ramanathan G, Yu C, Osei E, Nicolaides KH. Ultrasound examination at 37 weeks' gestation in the prediction of pregnancy outcome: the value of cervical assessment. Ultrasound Obstet Gynecol 2003;22:598-603.

20. Shynlova O, Tsui P, Dorogin A, Langille BL, Lye SJ. Insulin-like growth factors and their binding proteins define specific phases of myometrial differentiation during pregnancy in the rat. Biol Reprod 2007;76:571-8.