Human Reproduction, Vol.25, No.11 pp. 2894–2900, 2010
Advanced Access publication on July 19, 2010 doi:10.1093/humrep/deq177

human reproduction

ORIGINAL ARTICLE ***Reproductive epidemiology***

Health disparities in risk for cervical insufficiency

Emmanuel A. Anum [1], Haywood L. Brown [2], and Jerome F. Strauss III [1,*]

[1]Department of Obstetrics and Gynecology, Virginia Commonwealth University, Center on Health Disparities and Institute for Women's Health, MCV Campus, Sanger Hall, 1st Floor, Room 1-071, 1101 East Marshall Street, PO Box 980565, Richmond, VA 23298, USA
[2]Department of Obstetrics and Gynecology, Duke University, Durham, NC 27710, USA

*Correspondence address. Tel: +1-804-828-9788; Fax: +1-804-828-7628; E-mail: jfstrauss@vcu.edu

Submitted on May 2, 2010; resubmitted on June 10, 2010; accepted on June 15, 2010

BACKGROUND: The purpose of the study was to examine racial/ethnic differences in cervical insufficiency risk.

METHODS: We used the US 2005 Natality data file. Analysis was limited to singleton births. The prevalence of cervical insufficiency was examined by the maternal characteristic for each racial group. Unconditional logistic regression modeling was used to assess the association between race and cervical insufficiency while controlling for confounders.

RESULTS: Cervical insufficiency risk for Black women was more than twice that for their White counterparts [odds ratio (OR) (95% confidence interval (CI)) of 2.45 (2.22–2.71)]. Prior pregnancy termination showed a dose–response relationship with cervical insufficiency. Compared with women with no history of prior pregnancy termination, primiparous women who have had one pregnancy termination had an OR (95% CI) of 2.49 (2.23–2.77). The OR for two, three and four or more terminations were 4.66 (4.07–5.33), 8.07 (6.77–9.61) and 12.36 (10.19–15.00), respectively. Other predictors of cervical insufficiency included previous preterm birth, parity, marital status, renal disease, history of diabetes, polyhydramnios and anemia.

CONCLUSIONS: There were significant racial/ethnic disparities with Black women having increased cervical insufficiency risk, independent of other studied factors. Prior pregnancy termination is also a major risk factor for cervical insufficiency. The White/Black disparity is evident in both primiparous and multiparous women.

Key words: cervical insufficiency / pregnancy termination / race/ethnicity

Introduction

Preterm birth accounts for ~70% of all neonatal morbidity and mortality (Mathews and MacDorman, 2008). One of the known risk factors for preterm birth is cervical insufficiency. A cervix that shows a painless dilation and shortening during the second trimester of pregnancy with resultant recurrent pregnancy loss or delivery is considered incompetent (Norman, 2007). Ultrasound assessment of cervical length suggests that cervical sufficiency may be continuous with incompetence occupying the extreme end of a continuum (Warren and Silver, 2009).

About 27% of women with cervical insufficiency have been reported to have first-degree female relatives who also have cervical insufficiency (Warren *et al.*, 2007). Cervical insufficiency has been reported in pregnancies in women with the Ehlers–Danlos syndrome (Leduc and Wasserstrum, 1992; De Vos *et al.*, 1999) and Marfan syndrome (Paternoster *et al.*, 1998; Rahman *et al.*, 2003; Meijboom *et al.*, 2006; Tzialidou *et al.*, 2007). Polymorphisms in the COL1A1 and TGFB1 genes have been associated with cervical insufficiency.

Surgical and medical treatments such as cervical biopsy, treatment for cervical cancer, routine dilation and curettage for diagnostic and therapeutic purposes and termination of pregnancy, and trauma may all result in structural damage to the cervix, which may lead to cervical insufficiency. Forceful dilatation of the cervix performed during surgical procedures, and termination of pregnancy has the potential to damage the endocervix and result in cervical insufficiency, (Grunberger and Riss, 1979) and subsequent preterm delivery. The length of the cervix is an important risk factor in preterm delivery evaluation (Petrovic *et al.*, 2008) and the damage that repeated terminations may cause to the cervix includes shortening of the cervix. A short cervical length is a strong predictor of spontaneous preterm birth (Iams *et al.*, 1996; Goldenberg *et al.*, 2008). In a study among women with multiple prior-induced abortions, Visintine *et al.* (2008) reported preterm birth incidence of 47% in women with a short cervix (cervical length <25 mm) compared with 14% among those without a short cervix. Women who have had a prior spontaneous preterm delivery at <24 weeks have been found to have a higher incidence of cervical shortening compared with those whose preterm delivery was at a

later date (Szychowski *et al*., 2009). Cervical length has also been found to be highly predictive of preterm birth in twin gestations (To *et al*., 2006).

Although the association between cervical insufficiency and preterm birth is well established, no study has at yet examined cervical insufficiency rates and risk by race. Blacks have a higher preterm birth rate compared with Whites, and since having a preterm delivery is in itself a risk factor for cervical insufficiency, this study examined cervical insufficiency among primiparous women to determine if there are ethnic and racial differences in cervical insufficiency risk.

Materials and Methods

We used the US 2005 Natality data file that includes data based on the 1989 Revision of the US Standard Certificate of Live Birth for deliveries in 2004. The complete data set is available online at http://www.cdc.gov/nchs/data_access/VitalStatsOnline.htm#Period_Linked. Data from states that used the 2003 revised version of the Birth Certificate [Pennsylvania, South Carolina, Tennessee, Texas, Washington, Florida, Idaho, Kansas, Kentucky, New York (excluding New York City), Nebraska and New Hampshire] could not be used since information on cervical insufficiency, the outcome variable of interest, was only reported on the unrevised 1989 version of the Certificate of Live Birth. Cervical insufficiency is considered to be present if the term 'cervical incompetency' is checked on the birth certificate. The sample from New York City, the District of Columbia and the 37 states that used the unrevised Certificate represent 69% of all live births (ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/DVS/natality/UserGuide2005.pdf). Our analysis focused on primiparous women. All twins and any higher order gestations were excluded from the analysis. Records with missing information on cervical insufficiency were also excluded. The exposure variable was mother's race (given as White, Black, Asian/Pacific Islander or American Indian/Alaskan native). Covariates included mother's age and education level, marital status, number of prior pregnancy terminations, weight gain during pregnancy, maternal medical conditions (diabetes, pregnancy induced hypertension, anemia in pregnancy, hemoglobinopathy, genital herpes, renal disease or hydramnios), tobacco and alcohol use and adequacy of prenatal care. Mean ages and weight gain during pregnancy, and proportions of the various maternal characteristics were computed for each racial group. The prevalence of cervical insufficiency within each level of maternal characteristic was also assessed for each racial group. ORs for the association between each covariate and cervical insufficiency were computed. All clinically significant variables and any variable showing a *P*-value of 0.25 or less from the crude analysis were considered candidates for the multivariate model. Unconditional logistic regression modeling was used to assess the association between race and cervical insufficiency while controlling for confounders. Contribution of variables to the model was assessed by comparing the −2loglikelihood of the models with and without the covariate. Model adequacy was assessed using the Hosmer and Lemeshow Goodness-of-fit statistic. To check the stability of our effect estimates from the primiparous-only model, we fitted a second regression model that included women of all parity, controlling also for number of live births now living, number of live births now dead, and history of previous preterm birth. SAS 9.2 was used for statistical analysis.

Results

Of the 4 145 883 total live births recorded in 2004, 4 005 869 were singleton births. The number of singleton births based on the 1989 Revision of the US Standard Certificate of live birth was 2 771 890. Of this number, 1 115 541 were deliveries to primiparous women. A racial breakdown showed 852 296 (76.4%) were White, 166 966 (15.0%) were Black, 82 965 (7.4%) were Asian/Pacific Islanders and the rest were American Indians/Alaskan natives (Table I). Their mean ages ranged from 21.6 to 28.5 years. Approximately 0.23% of records had missing information on cervical insufficiency. The proportion of missing cervical insufficiency data among the different racial groups was 0.22% for Whites, 0.27% for Blacks, 0.23% for Asians and 0.66% for American Indians/Alaskan natives. Among preterm and term deliveries, the missing proportions were 0.34 and 0.21%, respectively. While 60.5% of Whites gave their marital status as 'married', among Blacks the proportion of married women was 21.9%. Asians/Pacific Islanders had the highest proportion of married women (81.3%). All racial groups had some fraction of their population with a history of at least one previous pregnancy termination. Blacks, however, had a significantly greater proportion of their population with two or more pregnancy terminations. Anemia in pregnancy was most prevalent in American Indians/Alaskan natives (4.2%) and least prevalent in Asians/Pacific Islanders (1.5%). Tobacco use during pregnancy was more prevalent among Whites and American Indians/Alaskan natives.

Approximately, one-half (49%) of all pregnancies among primiparous women with cervical insufficiency ended in preterm delivery. Of the preterm babies, 44% were delivered at 27 weeks of gestation or less. Cervical insufficiency prevalence and 95% confidence interval (95 % CI) for the different racial groups were 0.19% (0.19–0.20%) for Whites, 0.53% (0.49–0.56%) for Blacks, 0.18% (0.15–0.21%) for Asians/Pacific Islanders and 0.20% (0.14–0.30%) for American Indian/Alaskan natives (Table II). Cervical insufficiency prevalence showed an increasing trend with increasing number of pregnancy terminations. Whereas women with no history of pregnancy termination had a cervical insufficiency prevalence of 0.15%, among those with four or more terminations the prevalence was 3.15%. The cervical insufficiency prevalence associated with one, two and three pregnancy terminations were 0.46, 0.99 and 1.92%, respectively. High prevalence rates were also recorded in women with diabetes, hemoglobinopathies, renal disease and hydramnios. Women who had more than adequate prenatal care (i.e. the 'adequate plus' group) also had a high cervical insufficiency prevalence.

In the multivariate logistic regression that controlled for known cervical insufficiency risk factors, the adjusted cervical insufficiency risk for primiparous Black women was still more than twice that for their White counterparts [odds ratio (OR) (95% CI) of 2.45 (2.22–2.71)] (Table III). American Indians/Alaskan natives also had an OR (95% CI) of 1.62 (1.10–2.37) compared with Whites. The difference in cervical insufficiency risk between Whites and Asians/Pacific Islanders was not statistically significant. Pregnancy termination showed a strong association with cervical insufficiency, with the risk increasing as the number of previous pregnancy terminations increases. Compared with women with no history of prior pregnancy termination, primiparous women who have had one pregnancy termination had an OR (95% CI) of 2.49 (2.23–2.77). The ORs for two, three and four or more terminations were 4.66 (4.07–5.33), 8.07 (6.77–9.61) and 12.36 (10.19–15.00), respectively. Other strong predictors of cervical insufficiency were renal disease, history of diabetes, hydramnios and anemia. Compared with women who received adequate prenatal care, women who received adequate-plus care had an OR (95% CI)

Table I Maternal characteristics among primiparous women with singleton births by race, US 2005 Natality file.

Maternal characteristic	White	Black	Asian/Pacific Islander	American Indian/Alaskan Native
N	852 296	166 966	82 965	13 314
Mother's age*	25.4 (6.03)	22.8 (5.78)	28.5 (5.46)	21.6 (4.89)
Mother's education				
Some high school or less	159 359 (19.0%)	41 460 (25.2%)	6209 (7.6%)	4247 (32.3%)
High school graduate	237 711 (28.3%)	59 409 (36.2%)	15 479 (19.1%)	5194 (39.5%)
College	44 3770 (52.8%)	63 451 (38.6%)	59 537 (73.3%)	3717 (28.3%)
Married	516 009 (60.5%)	36 478 (21.9%)	67 457 (81.3%)	3459 (26.0%)
Previous pregnancy terminations				
None	716 447 (84.1%)	132 332 (79.4%)	70 096 (84.5%)	11 363 (85.4%)
One	100 919 (11.9%)	23 221 (13.9%)	9414 (11.4%)	1469 (11.0%)
Two	24 626 (2.9%)	7512 (4.5%)	2505 (3.0%)	355 (2.7%)
Three	6594 (0.8%)	2371 (1.4%)	652 (0.8%)	82 (0.6%)
Four or more	3133 (0.4%)	1326 (0.8%)	268 (0.3%)	38 (0.3%)
Anemia	13 978 (1.6%)	5425 (3.3%)	1242 (1.5%)	554 (4.2%)
Diabetes	23 301 (2.7%)	4301 (2.6%)	4521 (5.5%)	589 (4.5%)
Genital herpes	8746 (1.0%)	2202 (1.3%)	363 (0.4%)	105 (0.8%)
Hemoglobinopathy	378 (0.04%)	567 (0.34%)	89 (0.11%)	5 (0.04%)
Renal disease	2900 (0.34%)	284 (0.17%)	142 (0.17%)	54 (0.41%)
Hydramnios/oligohydramnios	13 682 (1.6%)	3593 (2.2%)	1365 (1.7%)	265 (2.0%)
Pregnancy induced hypertension	44 324 (5.2%)	8832 (5.3%)	2008 (2.4%)	896 (6.8%)
Tobacco use	72 197 (10.5%)	6961 (4.5%)	832 (1.6%)	1822 (15.0%)
Alcohol use	4981 (0.7%)	598 (0.4%)	161 (0.3%)	224 (1.8%)
Adequacy of prenatal care				
Inadequate	72 985 (8.8%)	24 018 (15.1%)	7405 (9.2%)	2555 (19.8%)
Intermediate	112 755 (13.6%)	23 445 (14.7%)	11 888 (14.8%)	2188 (16.9%)
Adequate	380 880 (45.9%)	60 907 (38.2%)	37 214 (46.3%)	4999 (38.7%)
Adequate plus	263 920 (31.8%)	51 099 (32.0%)	23 964 (29.8%)	3183 (24.6%)
Cervical insufficiency	1654 (0.19%)	876 (0.53%)	146 (0.18%)	27 (0.2%)
Weight gain during pregnancy*	33.3 (13.69)	31.0 (14.72)	31.2 (11.57)	33.5 (14.96)

*Mean (SD).
Cervical insufficiency is reported on the 1989 Revision of the US Certificate of Live Birth but not on the 2003 revised version. Thus, the analysis data set is only from States that report data based on the 1989 Revision of the US Certificate of Live Birth.

of 2.91 (2.64–3.22). This is not unexpected as women with cervical insufficiency and other high-risk medical conditions are more likely to begin prenatal care early and to have more prenatal visits. Their prenatal care index would thus seem to be more than adequate.

Alcohol use, unmarried status and weight gain during pregnancy each showed a reduction in incompetent cervix risk, but after fitting the logistic regression model for multiparous women, alcohol use was found not to be associated with an incompetent cervix (Table III). Blacks still showed an OR (95% CI) of 2.18 (2.02–2.36) compared with Whites after adjustment for multiparous women. This model also showed that the cervical insufficiency risk for Whites did not differ from that of the other two racial groups. Women with no college education also had a reduction in risk. Problems with small cell sizes may account for the unstable effect estimates that alcohol use and American Indians/Alaskan natives showed with the primiparous-only model. The model for multiparous women showed previous preterm birth, number of live births living and number of live births dead as strong predictors of cervical insufficiency. The strong positive trend associated with increasing number of pregnancy terminations was still evident.

Discussion

Disparities in preterm delivery between Blacks and Whites in the USA have existed for decades. Among the factors mentioned as contributing to these ethnic disparities are behavioral and socioeconomic factors, maternal stress, racism and genetic factors. Studies on the association of single gene defects with prematurity have provided evidence that genetic factors may also contribute to preterm birth (Anum *et al.*, 2009). The present analysis highlights that race/ethnicity differences exist in the diagnosis of cervical insufficiency, a cause of preterm delivery. The increased risk for cervical insufficiency among Black

Table II Prevalence of cervical insufficiency by maternal characteristics among primiparous women with singleton births, US 2005 Natality file.

Variable	Prevalence (%)	LL	UL	*P*-value
Race				<0.0001
White	0.19	0.19	0.20	
Black	0.53	0.49	0.56	
Asian/Pacific Islander	0.18	0.15	0.21	
American Indian/Alaskan native	0.20	0.14	0.30	
Previous pregnancy terminations				<0.0001
None	0.15	0.14	0.16	
One	0.46	0.43	0.50	
Two	0.99	0.89	1.10	
Three	1.92	1.66	2.21	
Four or more	3.15	2.68	3.69	
Mother's education				<0.0001
Some high school or less	0.17	0.15	0.19	
High school graduate	0.25	0.23	0.27	
College	0.27	0.26	0.28	
Marital status				0.003
Married	0.26	0.24	0.27	
Not-married	0.23	0.21	0.24	
Anemia				<0.0001
No	0.24	0.23	0.25	
Yes	0.39	0.31	0.48	
Diabetes				<0.0001
No	0.23	0.22	0.24	
Yes	0.72	0.64	0.82	
Pregnancy induced hypertension				0.001
No	0.24	0.23	0.25	
Yes	0.31	0.26	0.36	
Genital Herpes				<0.0001
No	0.24	0.23	0.25	
Yes	0.47	0.36	0.62	
Hemoglobinopathy				0.015*
No	0.24	0.23	0.25	
Yes	0.67	0.27	1.38	
Renal disease				0.0006
No	0.24	0.23	0.25	
Yes	0.53	0.32	0.84	
Hydramnios				<0.0001
No	0.24	0.23	0.25	
Yes	0.47	0.38	0.58	
Tobacco use				0.328
No	0.26	0.25	0.27	
Yes	0.24	0.21	0.28	
Alcohol use				0.056
No	0.26	0.25	0.27	
Yes	0.13	0.06	0.27	
Adequacy of prenatal care				<0.0001
Inadequate	0.14	0.12	0.17	
Intermediate	0.12	0.11	0.14	
Adequate	0.14	0.13	0.15	
Adequate plus	0.47	0.45	0.49	

Confidence intervals were computed with the Clopper-Pearson (exact) method. Two-sided *P*-values from Fisher's exact test (*). Where 25% or more of cells had expected counts less than five two-sided *P*-values from Fisher's exact test was reported.

women remained after controlling for other major risk factors, particularly prior pregnancy terminations.

It should be noted that cervical insufficiency is often a diagnosis of exclusion based upon a finding of advanced cervical dilatation or history of pregnancy loss (Craigo, 1996). Moreover, the diagnosis of cervical insufficiency was not made by standardized criteria across all obstetrical services. This represents a limitation of our study. It is possible that women who delivered preterm would be more likely to check cervical insufficiency on the birth certificate as a complication compared with women who had cervical changes earlier in pregnancy, but delivered at term. Women with a history of multiple prior pregnancy terminations who delivered preterm may also be more likely to check cervical insufficiency as a complication. American Indians/Alaskan natives had the highest proportion of missing cervical insufficiency data, but there were no significant differences in the proportion missing among the other racial groups. The diagnosis of cervical insufficiency can be challenging in women having their first delivery, and this may result in cases of the condition not having been captured on the birth certificate. There may also be under reporting of the number of previous pregnancy terminations. These factors also represent limitations of this study. It should also be noted that there is a high likelihood of blank responses to some variables on the birth certificate, which would lead to a list-wise deletion of such records in a logit model. In this study, however, over 80% of all the records were utilized in the multivariate logistic regression model.

Although findings on the association between prior pregnancy termination and subsequent preterm delivery have been mixed (Pickering and Forbes, 1985; Henriet and Kaminski, 2001; Moreau *et al.*, 2005; Raatikainen *et al.*, 2006; Virk *et al.*, 2007; Brown *et al.*, 2008; Voigt *et al.*, 2008, 2009; Freak-Poli *et al.*, 2009), the observed 'dose–response relationship' between number of pregnancy terminations and preterm risk, as demonstrated in a recent meta-analysis by Shah and Zao (2009) provides strong evidence in favor of an association between pregnancy termination and preterm birth. The strong association between prior pregnancy termination and cervical insufficiency irrespective of race/ethnicity was confirmed in our analysis. This relationship is presumed to be due to cervical trauma from the

Table III Crude and adjusted OR (95% CI) for cervical insufficiency by maternal characteristic among singleton live births, US 2005 Natality file.

Variable	Crude OR	Adjusted OR*	Adjusted OR**
Race (ref = White)			
Black	2.66 (2.43–2.90)	2.45 (2.22–2.71)	2.18 (2.02–2.36)
Asian/Pacific Islander	1.10 (0.90–1.34)	0.96 (0.79–1.18)	0.97 (0.81–1.16)
American Indian/Alaskan Native	1.16 (0.79–1.70)	1.62 (1.10–2.37)	1.02 (0.75–1.38)
Pregnancy terminations (ref = 0)			
1	2.80 (2.53–3.12)	2.49 (2.23–2.77)	1.71 (1.57–1.85)
2	6.03 (5.30–6.87)	4.66 (4.07–5.33)	2.86 (2.60–3.16)
3	12.12 (10.26–14.32)	8.07 (6.77–9.61)	3.55 (3.10–4.06)
4+	20.76 (17.31–24.91)	12.36 (10.19–15.00)	5.96 (5.24–6.78)
Mother's age	1.06 (1.06–1.07)	1.03 (1.03–1.04)	1.02 (1.02–1.03)
Marital status: not married versus married	0.87 (0.80–0.95)	0.89 (0.80–0.99)	0.80 (0.73–0.87)
Alcohol use	0.41 (0.18–0.91)	0.37 (0.17–0.84)	1.00 (0.69–1.44)
History of diabetes	3.04 (2.63–3.53)	1.69 (1.45–1.98)	1.30 (1.15–1.47)
Pregnancy-induced hypertension	1.19 (1.01–1.41)	1.02 (0.86–1.21)	0.90 (0.76–1.06)
Anemia in pregnancy	1.55 (1.22–1.96)	1.38 (1.08–1.75)	1.25 (1.05–1.49)
Genital herpes	1.88 (1.41–2.51)	1.25 (0.93–1.68)	1.57 (1.25–1.96)
Renal disease	2.26 (1.40–3.64)	2.21 (1.36–3.59)	1.61 (1.10–2.35)
Hydramnios/oligohydramnios	1.97 (1.58–2.47)	1.48 (1.18–1.86)	1.39 (1.13–1.71)
Mother's education level (ref = college)			
Some High school or less	0.58 (0.50–0.66)	0.93 (0.79–1.08)	0.66 (0.59–0.74)
High school graduate	0.90 (0.82–0.99)	1.05 (0.95–1.17)	0.86 (0.80–0.94)
Prenatal care adequacy (ref = adequate)			
Inadequate	1.04 (0.87–1.26)	1.00 (0.82–1.21)	0.70 (0.59–0.82)
Intermediate	0.93 (0.78–1.10)	0.88 (0.73–1.05)	0.80 (0.70–0.92)
Adequate plus	3.41 (3.09–3.76)	2.91 (2.64–3.22)	2.57 (2.38–2.78)
Weight gain during pregnancy	0.97 (0.96–0.97)	0.97 (0.97–0.98)	0.99 (0.99–0.99)
Previous preterm birth			8.16 (7.49–8.89)
Live births now living (ref = three or more)			
0			4.18 (3.48–5.02)
1			1.77 (1.60–1.97)
2			1.38 (1.24–1.55)
Live births now dead (ref = 0)			
One			4.90 (4.38–5.48)
Two or more			5.69 (4.69–6.90)

*Primiparous-only model; Hosmer and Lemeshow Goodness-of-fit test: *P*-value = 0.18.
**Model with multiparous women. Cervical insufficiency is reported on the 1989 Revision of the US Certificate of Live Birth but not on the 2003 revised version. Thus, analysis data set is only from States that report data based on the 1989 Revision of the US Certificate of Live Birth.

procedures. However, there are a number of relevant questions that cannot be addressed in our study because information was not available, including whether the gestational age at which pregnancies were terminated influences risk of cervical insufficiency, whether the method and protocol for the procedures is a determinant of risk, and whether the technical skill of the operator is a factor.

The association between risk for cervical insufficiency and diabetes, and renal disease may reflect the biochemical sequela of glucose intolerance that influence tissue proteins. Post-translational modification of tissue proteins (glycation) associated with hyperglycemia could influence the structural integrity of the cervix. For example, collagen glycation is known to occur in diabetes and is associated with diabetic renal disease (Valcourt *et al*., 2007; Sell *et al*., 2010). Thus, there is precedent for non-enzymatic post-translational protein modification affecting extracellular matrix function. The relationship between protein glycation and cervical insufficiency merits further evaluation.

Alternatively, the association between diabetes and cervical insufficiency could reflect the impact of body composition, assuming that obesity is a factor contributing to diabetes and associated diabetic nephropathy. African-American women have higher obesity rates in

pregnancy than women of other races (Salihu *et al*., 2009). Since body mass index was not available in the databases queried, we could not test for associations between cervical insufficiency and obesity. However, in a study of obese German women, cervical insufficiency was less frequent in the obese population (Briese *et al*., 2010).

The risk differences for cervical insufficiency among ethnic groups could be explained by environmental factors not assessed in our study, such as infection leading to inflammatory changes in the cervix. The incidence of sexually transmitted diseases and bacterial vaginosis is higher in Blacks than Whites (Goldenberg *et al*., 1996; Centers for Disease Control and Prevention, 2007) and this may be one contributing factor to the increased risk among Blacks.

Genetic factors might also contribute to increased risk for cervical insufficiency among Blacks. However, at present, there are no known genetic variants that can explain this increased risk. It is of interest to note that pelvic organ prolapse is less frequent in Black women than in White women (Nygaard *et al*., 2008; Weiss *et al*., 2009; Whitcomb *et al*., 2009; Sears *et al*., 2009; Chen *et al*., 2010). Thus, if variation in genes encoding proteins involved in maintaining tissue integrity in the pelvic floor and reproductive tract are involved, the disparate risks for cervical insufficiency and pelvic floor dysfunction would predict that the gene effects were highly specific to the uterine cervix.

In conclusion, our results strongly suggest that prior pregnancy termination is a major risk factor for cervical insufficiency. However, we found significant racial/ethnic disparities with both primiparous and multiparous Black women having an increased risk independent of the influence of prior pregnancy terminations. This increased risk among Blacks contributes to the racial/ethnic disparities in preterm birth. The underlying cause(s) for the disparity in risk of cervical insufficiency are not known, but could include environmental factors (reproductive tract infection/inflammation), biochemical changes resulting from comorbid conditions (diabetes), and yet to be defined genetic factors.

Funding

This work was supported by NIH P60 MD002256 and RO1 HD34612.

References

Anum EA, Springel EH, Shriver MD, Strauss JF III. Genetic contributions to disparities in preterm birth. *Pediatr Res* 2009;**65**:1–9.

Briese V, Voigt M, Wisser J, Borchardt U, Straube S. Risks of pregnancy and birth in obese primiparous women: an analysis of German perinatal statistics. *Arch Gynecol Obstet* 2010 [Epub ahead of print].

Brown JS Jr, Adera T, Masho SW. Previous abortion and the risk of low-birth weight and preterm births. *J Epidemiol Community Health* 2008;**62**:16–22.

Centers for Disease Control and Prevention, Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Trends in Reportable Sexually Transmitted Diseases in the United States, 2007. http://www.cde.gov/std/stats07/trends.htm.

Chen C, Hill LD, Schubert CM, Strauss JF III., Matthews CA. Is laminin gamma-1 a candidate gene for advanced pelvic organ prolapse? *Am J Obstet Gynecol* 2010 [Epub ahead of print].

Craigo SD. Cervical incompetence and preterm delivery. *N Engl J Med* 1996;**334**:595–596.

De Vos M, Nuytinck L, Verellen C, De Paepe A. Preterm premature rupture of membranes in a patient with the hypermobility type of the Ehlers–Danlos syndrome. A case report. *Fetal Diagn Ther* 1999; **14**:244–247.

Freak-Poli R, Chan A, Tucker G, Street J. Previous abortion and risk of preterm birth: a population study. *J Matern Fetal Neonatal Med* 2009; **22**:1–7.

Goldenberg RL, Klebanoff MA, Nugent R, Krohn MA, Hillier S, Andrews WW. Bacterial colonization of the vagina during pregnancy in four ethnic groups. Vaginal Infections and Prematurity Study Group. *Am J Obstet Gynecol* 1996;**174**:1618–1621.

Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet* 2008;**371**:75–84.

Grunberger W, Riss P. Cervical incompetence after previous cervical dilatation and curettage (author's transl). *Wien Med Wochenschr* 1979; **129**:390–392.

Henriet L, Kaminski M. Impact of induced abortions on subsequent pregnancy outcome: the 1995 French national perinatal survey. *BJOG* 2001;**108**:1036–1042.

Iams JD, Goldenberg RL, Meis PJ, Mercer BM, Moawad A, Das A, Thom E, McNellis D, Copper RL, Johnson F *et al*. The length of the cervix and the risk of spontaneous premature delivery. *N Engl J Med* 1996; **334**:567–572.

Leduc L, Wasserstrum N. Successful treatment with the Smith-Hodge pessary of cervical incompetence due to defective connective tissue in Ehlers–Danlos syndrome. *Am J Perinatol* 1992;**9**:25–27.

Mathews TJ, MacDorman MF. *Infant mortality statistics from the 2005 period linked birth/infant death data set*. National Vital Statistics Reports; **57** (2). Hyattsville, MD: National Center for Health Statistics, 2008.

Meijboom LJ, Drenthen W, Pieper PG, Groenink M, van der Post JA, Timmermans J, Voors AA, Roos-Hesselink JW, van Veldhuisen DJ, Mulder BJ *et al*. Obstetric complications in Marfan syndrome. *Int J Cardiol* 2006;**110**:53–59.

Moreau C, Kaminski M, Ancel PY, Bouyer J, Escande B, Thiriez G, Boulot P, Fresson J, Arnaud C, Subtil D *et al*. Previous induced abortions and the risk of very preterm delivery: results of the EPIPAGE study. *BJOG* 2005;**112**:430–437.

Norman JE. Preterm labour. Cervical function and prematurity. *Best Pract Res Clin Obstet Gynaecol* 2007;**21**:791–806.

Nygaard I, Barber MD, Burgio KL, Kenton K, Meikle S, Schaffer J, Spino C, Whitehead WE, Wu J, Brody DJ *et al*. Prevalence of symptomatic pelvic floor disorders in US women. *JAMA* 2008;**300**:1311–1316.

Paternoster DM, Santarossa C, Vettore N, Dalla Pria S, Grella P. Obstetric complications in Marfan's syndrome pregnancy. *Minerva Ginecol* 1998; **50**:441–443.

Petrovic D, Novakov-Mikic A, Mandic V. Socio-demographic factors and cervical length in pregnancy. *Med Pregl* 2008;**61**:443–451.

Pickering RM, Forbes JF. Risks of preterm delivery and small-for-gestational age infants following abortion: a population study. *Br J Obstet Gynaecol* 1985;**92**:1106–1112.

Raatikainen K, Heiskanen N, Heinonen S. Induced abortion: not an independent risk factor for pregnancy outcome, but a challenge for health counseling. *Ann Epidemiol* 2006;**16**:587–592.

Rahman J, Rahman FZ, Rahman W, al-Suleiman SA, Rahman MS. Obstetric and gynecologic complications in women with Marfan syndrome. *J Reprod Med* 2003;**48**:723–728.

Salihu HM, Luke S, Alio AP, Wathington D, Mbah AK, Marty PJ, Whiteman V. The superobese mother and ethnic disparities in preterm birth. *J Natl Med Assoc* 2009;**101**:1125–1131.

Sears CL, Wright J, O'Brien J, Jezior JR, Hernandez SL, Albright TS, Siddique S, Fischer JR. The racial distribution of female pelvic floor disorders in an equal access health care system. *J Urol* 2009;**181**:187–192.

Sell DR, Nemet I, Monnier VM. Partial characterization of the molecular nature of collagen-linked fluorescence: role of diabetes and end-stage renal disease. *Arch Biochem Biophys* 2010;**493**:192–206.

Shah PS, Zao J, Knowledge Synthesis Group of Determinants of preterm/LBW births. Induced termination of pregnancy and low birthweight and preterm birth: a systematic review and meta-analyses. *BJOG* 2009;**116**:1425–1442.

Szychowski JM, Owen J, Hankins G, Iams J, Sheffield J, Perez-Delboy A, Berghella V, Wing DA, Guzman ER; Vaginal Ultrasound Cerclage Trial Consortium. Timing of mid-trimester cervical length shortening in high-risk women. *Ultrasound Obstet Gynecol* 2009;**33**:70–75.

To MS, Fonseca EB, Molina FS, Cacho AM, Nicolaides KH. Maternal characteristics and cervical length in the prediction of spontaneous early preterm delivery in twins. *Am J Obstet Gynecol* 2006;**194**:1360–1365.

Tzialidou I, Oehler K, Scharf A, Staboulidou I, Westhoff-Bleck M, Hillemanns P, Günter HH. Marfan syndrome in pregnancy: presentation of four cases and discussion. *Z Geburtshilfe Neonatol* 2007;**211**:36–41.

Valcourt U, Merle B, Gineyts E, Viguet-Carrin S, Delmas PD, Garnero P. Non-enzymatic glycation of bone collagen modifies osteoclastic activity and differentiation. *J Biol Chem* 2007;**282**:5691–5703.

Virk J, Zhang J, Olsen J. Medical abortion and the risk of subsequent adverse pregnancy outcomes. *N Engl J Med* 2007;**357**:648–653.

Visintine J, Berghella V, Henning D, Baxter J. Cervical length for prediction of preterm birth in women with multiple prior induced abortions. *Ultrasound Obstet Gynecol* 2008;**31**:198–200.

Voigt M, Olbertz D, Fusch C, Krafczyk D, Briese V, Schneider KT. The influence of previous pregnancy terminations, miscarriages and still-births on the incidence of babies with low-birth weight and premature births as well as a somatic classification of newborns. *Z Geburtshilfe Neonatol* 2008;**212**:5–12.

Voigt M, Henrich W, Zygmunt M, Friese K, Straube S, Briese V. Is induced abortion a risk factor in subsequent pregnancy? *J Perinat Med* 2009;**37**:144–149.

Warren JE, Silver RM. Genetics of the cervix in relation to preterm birth. *Semin Perinatol* 2009;**33**:308–311.

Warren JE, Silver RM, Dalton J, Nelson LT, Branch DW, Porter TF. Collagen 1Alpha1 and transforming growth factor-beta polymorphisms in women with cervical insufficiency. *Obstet Gynecol* 2007;**110**:619–624.

Weiss G, Noorhasan D, Schott LL, Powell L, Randolph JF Jr, Johnston JM. Racial differences in women who have a hysterectomy for benign conditions. *Womens Health Issues* 2009;**19**:202–210.

Whitcomb EL, Rortveit G, Brown JS, Creasman JM, Thom DH Van Den Eeden SK, Subak LL. Racial differences in pelvic organ prolapse. *Obstet Gynecol* 2009;**114**:1271–1277.