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# Maternal body mass index and cervical length among women with a history of spontaneous preterm birth†

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## Abstract

**Objectives:** To evaluate whether women with a prior spontaneous preterm birth (SPTB) with a higher body mass index (BMI) have a lower risk of a shortened cervix in a subsequent pregnancy.

**Study Design:** A secondary analysis of the Maternal-Fetal Medicine Units Network RCT of omega-3 fatty acid supplementation for recurrent SPTB prevention. All women had ≥1 prior SPTB <37 weeks, a singleton pregnancy, and initiated 17-alpha hydroxyprogesterone caproate(17-OHPC). The primary exposure was pre-pregnancy BMI. The primary outcome was the shortest transvaginal cervical length <30 mm.

**Results:** Of the 356 women with a prior SPTB receiving 17-OHPC and a cervical length available, 108 (30%) were overweight and 103 (29%) obese; 12% had a cervical length <30 mm. Fewer overweight/obese women had a shortened cervix compared to normal-weight women (43 versus 57%; odds ratio: 0.47 [95%CI: 0.25–0.89]). After adjusting for maternal age, number of prior SPTBs, and tobacco use, overweight/obese women were less than half as likely to have a shortened cervix compared to normal-weight women (adjusted odds ratio: 0.46, 95%CI: 0.24–0.89).

**Conclusions:** Overweight and obese women with a prior SPTB receiving 17-OHPC have longer cervical lengths compared to normal weight women, and this finding could explain a possible mechanism between the decreased rate of SPTB and larger BMI.

### Keywords

Body mass index; cervical length; obesity; preterm birth; short cervix

## Introduction

Obesity and cervical insufficiency are leading causes of morbidity in pregnancy [1,2]. In the USA, over 1 in 5 women of reproductive age are obese (body mass index, BMI >30 kg/m$^2$),

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Disclosure statement

No potential conflict of interest was reported by the authors.

and the rate of obesity continues to rise [3]. Preterm birth (PTB) accounts for approximately 12% of live births in the US and is the principal cause of infant mortality in non-anomalous neonates, leading to over >30% of infant deaths [4,5]. Women with a prior spontaneous PTB (SPTB) are at an exceedingly high risk for recurrent PTB in subsequent pregnancies; use of 17-alpha hydroxyprogesterone caproate (17-OHPC) prophylaxis has been shown to reduce the rate of singleton PTB in women with a prior SPTB [6].

The data regarding the risk of SPTB in overweight and obese women is conflicting; some studies show an increased risk of SPTB, while other studies show that overweight and obese women have a decreased risk of SPTB compared to normal-weight women [7–10]. Cervical length is an established risk factor for SPTB [5]. Prior observational data suggest that overweight and obese women may have a longer mid trimester cervical length compared to normal-weight women [11–17]. However, these data were limited as some did not adjust for confounders. In addition, the two most recent studies (Venkatesh et al., and Palatnik et al.) were limited as the first study included transabdominal rather than uniform transvaginal assessment cervical length assessments and both studies were not restricted to high-risk pregnant women with a history of prior SPTB [11,12]. Hence, there are currently limited data available evaluating the association between BMI and cervical length using transvaginal cervical length assessment among pregnant women at the highest risk for a mid trimester short cervix, namely those with a history of prior SPTB receiving 17-OHPC.

We hypothesized that among this high-risk cohort of pregnant women, those with a higher BMI would have longer second trimester cervical lengths. The aim of the current study was to evaluate whether overweight and obese women with a history of a prior SPTB have a lower risk of developing a short cervix in a subsequent pregnancy compared to normal-weight women.

## Materials and methods

This is a secondary analysis of pregnant women enrolled in the Eunice Kennedy Shriver National Institutes of Child Health and Human Development Maternal Fetal Medicine Units Network multicenter randomized, double-blind, placebo-controlled trial of omega-3 fatty acid supplementation versus placebo for recurrent PTB prevention [18]. Briefly, women with a history of a prior SPTB between 20 and <37 weeks of gestation and a current singleton gestation were assigned to either a daily omega-3 fatty acid supplement or a matching placebo from 16 and <22 weeks of gestation. All women received weekly intramuscular 17-OHPC (250 mg) in clinic provided through the original trial as described by Meis et al. [6]. Pregnancies were dated by a previously described algorithm on the basis of the last menstrual period and earliest ultrasound examination [19]. All outcomes were reviewed by trained research nurses at the time of the original study. This study found no association between omega-3 fatty acid supplementation and recurrent PTB risk (relative risk, RR 0.91, 95% CI 0.77–1.07) [18]. This secondary analysis of de-identified publicly available data was exempt from Institutional Review Board approval.

Women were included in the current analysis if they met original trial criteria (i.e. ≥1 prior SPTB <37 weeks of gestation, a singleton pregnancy, and initiated 17-OHPC at 16–20 weeks of gestation) and had a transvaginal cervical length assessment between 14 – <23 weeks of gestation. Pre-pregnancy weight and current height were assessed for each woman at the initial study visit (median 10 weeks of gestation). BMI was calculated by dividing her weight in kilograms by the square of her height in meters ($kg/m^2$). Women were then grouped by BMI category using World Health Organization (WHO) criteria, namely normal range (18.5 – <25 $kg/m^2$), overweight (25 – <30 $kg/m^2$), and obese (≥30$kg/m^2$) [20]. BMI was also evaluated as a continuous linear variable. Demographic variables included: age, race/ethnicity, education, parity, and any tobacco use during pregnancy.

The primary exposure was overweight or obese women compared to normal-weight women, which was assessed at the initial study visit (i.e. pre-pregnancy BMI). The primary outcome was the development of a transvaginal cervical length <30 mm between 14 weeks 0 days and 22 weeks 6 days of gestation. The cut-off of 30 mm is based on the Iams et al. study and also the Owen et al. study [10,21]. In the Owen study, women with a prior PTB and a cervical length <30 mm had a PTB rate of 26%; use of 30 versus 25 mm at 16–18 weeks in this high risk population increased the sensitivity of using cervical length as a predictor for SPTB [21].

We calculated descriptive statistics for the study population of women overall and then separately for overweight or obese women versus those with a normal weight (BMI <25.0 $kg/m^2$ vs. ≥25.0 $kg/m^2$). Confounding variables were selected based on an *a priori* review of the literature as well as based on univariate statistical significance ($p < .10$) [22]. Logistic regression models were used to compare demographic and clinical characteristics of women; and adjusted odds ratios (aOR) were calculated for covariates associated with a cervical length <30 mm. For all multivariable models, individual predictor variables with $p < .20$ were retained in final models. Initial multivariable models were adjusted for maternal age, number of prior SPTBs, tobacco use, and self-reported race. Black race was removed from the final multivariable model for $p \geq .20$. We conducted the following sensitivity analyses: (1) assessment of both cervical length and BMI as continuous measures using multivariable linear regression analyses; and (2) exclusion of 14 women who had either a cerclage placed in the current pregnancy and/or a diagnosed uterine anomaly. All analyses used Stata (StataCorp, version 10.0, College Station, TX, USA).

## Results

Of the 852 enrolled women in the original trial, 356 (42%) women with a history of a prior SPTB receiving 17-OHPC had a transvaginal ultrasound measuring cervical length between 14 – <23 weeks. The remaining 496 women were excluded from this study due to a cervical length assessment <14 weeks ($n$ = 24), no cervical length assessment ($n$ = 468), or a missing BMI ($n$ = 4). Women in this secondary analysis ($n$ = 356) were similar to excluded women ($n$ = 496) with regards to maternal age, African American race, number of prior SPTBs, and gestational age at delivery (all $p > .05$); however, women included in the current analysis were more likely to smoke during pregnancy (20 versus 13%; $p < .01$) and were more likely to be overweight or obese (59 versus 47%; $p < .001$) compared to excluded women.

Among the 356 women, the mean pre-pregnancy BMI was 27.4 (standard deviation, SD 6.76). Two-fifths of women (40%, 145/356) were normal weight (BMI <25.0 kg/m$^2$), 108/356 (30%) were overweight (BMI 25.0 – <30 kg/m$^2$), and 103/356 (29%) were obese (BMI ≥30kg/m$^2$). The mean age was 27.8 years (SD 5.25). Over a fourth of women (26%) had two or more prior SPTBs, 44% (156/356) self-identified as white race, and 20% (70/356) reported using tobacco. A total of 11 women (3%) had a cerclage placed during the current pregnancy. The mean gestational age at delivery was 36.2 weeks (SD 4.46). Forty-one percent of women (147/356) had a recurrent PTB <37 weeks, among whom 82% (121/147) were recurrent SPTB <37 weeks.

Table 1 presents baseline demographic and clinical data comparing 211 overweight and obese women to their 145 normal-weight counterparts. Black women were more likely to be overweight and obese compared to white women (47 versus 23%; $p < .001$). No other significant differences were noted by BMI. Though overweight/obese women were less likely to have a recurrent SPTB <37 weeks compared to normal-weight women, this was not a significant difference (32 versus 37%; $p = .28$).

A total of 12% (44/356) of women had a cervical length <30 mm. The mean cervical length was 38 mm (SD 8.01). The median cervical length was 37 and 42 mm at the 75th percentile and 33 mm 25th percentile, respectively. Cervical length was assessed by transvaginal ultrasound between 14 and <23 weeks at a mean gestational age of 18.0 weeks (SD 1.76), which did not differ between overweight and obese versus normal-weight women (18.1 versus 17.9 weeks).

In univariate analyses, when cervical length was defined as a short cervix <3.0 cm, fewer overweight and obese women had a shortened cervix compared to normal-weight women (43 versus 57%; OR: 0.47 [95% CI: 0.25–0.89]). Women with multiple (i.e. ≥2) prior SPTBs were less likely to have a shortened cervix compared to women with only one prior SPTB (18 versus 27%; OR: 0.47 [95% CI: 0.25–0.89]). There were no significant differences in cervical length by maternal age, race, or tobacco use.

In multivariable analyses, after adjusting for maternal age, number of prior SPTBs, and tobacco use, overweight and obese women were less than half as likely to have a shortened cervix <3.0 cm compared to normal-weight women (adjusted odd ratio, aOR: 0.46, 95% CI: 0.24–0.89).

In sensitivity analyses, after adjusting for the same covariates as above, when cervical length and BMI were assessed as continuous variables in a multivariable linear regression model, for each 1.0 kg/m$^2$ increase in BMI, cervical length increased by 0.13 mm (95% CI: 0.01–0.25). In addition, obese and overweight women were less likely to have a shortened cervix <30 mm compared to normal-weight women after excluding the 11 women who had a cerclage placed during the current pregnancy or a diagnosed uterine anomaly (aOR: 0.45, 95% CI: 0.23–0.86).

## Discussion

We found that overweight and obese pregnant women with a prior SPTB receiving 17-OHPC in a subsequent pregnancy had a longer mid trimester cervical length compared to normal-weight women. Overweight and obese women at high risk for recurrent SPTB were less than half as likely to have a shortened cervix <30 mm, after adjusting for the number of prior SPTBs and other confounders. Future studies conducted among women at high risk for SPTB are needed to determine if these findings reflect a possible mechanism to explain the decreased rate of SPTB in women with a larger BMI.

While prior observational studies have noted a similar relationship between maternal BMI and mid-trimester cervical length, they were not conducted among the subpopulation of women at high risk for SPTB. A recent analysis including >18,000 women without a prior SPTB who underwent routine mid trimester transvaginal cervical length assessment found that a higher BMI was associated with a longer mid trimester cervical length, and correspondingly reduced SPTB. However, the decreased risk of SPTB was not associated with cervical length [12]. A secondary analysis of a trial evaluating cerclage for women with a short cervix <25 mm and a prior SPTB <34 weeks found that BMI was not associated with cervical length measured between 16 and 23 weeks nor gestational age at birth [16]. Prior observational data have noted an association between longer cervical length and higher BMI [11,14,15,17], but not consistently [23]. In addition, some studies have found that maternal obesity is associated with a decreased rate of SPTB [8], though the opposite association has also been observed in recent studies, including among women with a prior SPTB receiving 17-OHPC [24–26]. Altogether, these findings suggest that maternal obesity early in pregnancy may be associated with a longer cervical length, and could be one possible mechanism for a protective effect of obesity on PTB, however, any such mechanism is likely multifactorial and may vary based on the baseline risk of PTB of the study population.

The difference in cervical length between overweight and obese versus normal-weight women may not necessarily explain the clinical association between BMI and SPTB. For instance, the difference in cervical length between overweight and obese versus normal weight women was only 0.20 cm, which is consistent with the numerically small difference (0.18 cm) in cervical length associated with obesity in prior studies [12]. An explanation for why pregnant women with a higher BMI may have a longer cervical length remains to be elucidated. Obese women may have a different physiology, inflammatory milieu, endocrine environment, soft tissue in the maternal pelvis, and profile of comorbid conditions compared to their normal-weight counterparts, all of which could influence cervical length [27]. Recent strategies have aimed to improve the discriminatory ability of cervical length assessment by limiting screening to low risk women with identifiable risk factors for a short cervix, including minority race, tobacco use, prior preterm birth, and prior cervical procedure [28]; and BMI could be considered as an additional risk factor for short cervix in this algorithm in the future. It should be noted that the high-risk women in the current study would warrant cervical length screening regardless of BMI given their prior history of SPTB.

In unadjusted analyses, women with a history of more than one prior SPTB were less likely to develop a short cervix, but this association did not hold after adjustment for other confounders. Given the etiology of SPTB is likely multifactorial and the relative importance of risk factors may change with the number of prior SPTB, it is possible that the impact of short cervix on SPTB varies between women with one versus multiple prior SPTB.

This study must be interpreted within the context of its design. The current study is a secondary analysis of a RCTthat was not designed with this particular endpoint in mind. We are unable to comment on why some women did not have a documented transvaginal mid trimester cervical length. The pressure placed by the vaginal probe can impact the cervical length. Hence, it is possible that obese women might require more pressure or a deeper insertion of the probe to ascertain the cervical length measurement. Some factors previously found to be associated with short cervical length were not available in this dataset, including prior history of uterine evacuation [29] and excisional procedures of the cervix [30]. The proportion of women who were overweight and obese in the current study was consistent with the wider population of pregnant women in the US [3,31]. These results will need to be replicated in larger cohorts of high-risk women with a history of a prior SPTB receiving 17-OHPC undergoing universal transvaginal ultrasound screening of second trimester cervical length before these results can be generalized further. In addition, whether cervical length mediates the relationship between BMI and SPTB among women at high risk for recurrent SPTB will need to be studied.

A strength of this study is we assessed a group of pregnant women at high risk for recurrent SPTB who were receiving 17-OHPC who may be different than earlier studies that were conducted among low-risk cohorts. We were able to control for important variables associated with cervical length in the current analysis, namely history of prior SPTB, which was one of the inclusion criteria, and uterine anomaly and cerclage placement, for which women were excluded in sensitivity analyses. The study outcome was based on transvaginal cervical length assessment, and it is important to note that some prior studies have utilized transabdominal cervical length assessment, which may overestimate cervical shortening compared to transvaginal sonography [32,33]. We chose a cervical length cut-off of 30 mm, which was consistent with prior observational data assessing the relationship between cervical length and SPTB [10,22]. Future studies with a larger sample size of high-risk women will be needed to further compare overweight to obese women, as well as to assess impact of obesity with greater granularity (such as higher thresholds of BMI >40).

In conclusion, this study identified a significant association between maternal BMI and second trimester cervical length among women at high risk for recurrent SPTB receiving 17-OHPC prophylaxis. Despite the many deleterious clinical consequences of maternal obesity in pregnancy, these results do suggest that overweight and obese women are more likely to have a longer cervical length compared to normal-weight women. Given that over half of US women of childbearing age are overweight or obese, these findings have implications for the assessment of second trimester cervical length, and possibly for more distal pregnancy outcomes mediated by cervical length.

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## Table 1.

Baseline maternal characteristics by BMI comparing overweight/obese women versus normal weight women ($N = 356$).

| Maternal characteristics | Overall $N$ = 356 $n$ (%) | Overweight/obese, ≥25 kg/m$^2$ N = 211 $n$ (%) | Normal, <25 kg/m$^2$ $N$ = 145 $n$ (%) | $p$-Value |
|---|---|---|---|---|
| Mean age (SD), years | 27.8 (5.25) | 28.2 (5.31) | 27.3 (5.11) | .08 |
| Number of prior SPTBs ≥2 | 92 (25.8) | 60 (28.4) | 32 (22.1) | .17 |
| Race | | | | |
| White | 156 (43.8) | 72 (34.1) | 84 (57.9) | <.001 |
| Black | 132 (37.1) | 99 (46.9) | 33 (22.8) | |
| Hispanic/Latina | 60 (16.9) | 36 (17.1) | 24 (16.6) | |
| Other | 8 (2.3) | 4 (1.9) | 4 (2.8) | |
| Education >12 years | 98 (46.5) | 98 (46.5) | 79 (54.5) | .13 |
| Tobacco use | 70 (19.7) | 44 (20.9) | 26 (17.9) | .49 |
| Cerclage in current pregnancy | 11 (3.1) | 7 (3.3) | 4 (2.8) | .76 |
| Mean cervical length (SD), mm | 37 (8.01) | 38 (7.49) | 36 (8.60) | .01 |
| Mean gestational age of TVUS for cervical length (SD), weeks | 18.0 (1.76) | 18.1 (1.75) | 17.9 (1.77) | .29 |

All frequencies reflect column percentages.

**Table 2.**

Multivariable analysis of maternal characteristics associated with a short cervix (<30 mm).

| Maternal characteristic | Overall *N* = 356 *n* (%) | Short cervix *N* = 44 *n* (%) | No short cervix *N* = 312 *n* (%) | Unadjusted odds ratio, OR (95% CI)[a] | Adjusted odds ratio, a OR (95% CI)[a,b] |
|---|---|---|---|---|---|
| Prepregnancy BMI, $kg/m^2$ [b] | | | | | |
| Overweight/obese, ≥25 | 211 (59.3) | 19 (43.2) | 192 (61.5) | **0.47 (0.25–0.89)** | **.46 (.24–.89)** |
| Normal <25 | 145 (40.7) | 25 (56.8) | 120 (38.5) | 1.00 | 1.00 |
| Age[b] | | | | | |
| <25 years | 92 (25.8) | 9 (20.5) | 83 (26.6) | 0.70 (0.32–1.53) | .57 (.26–1.26) |
| ≥25 years | 264 (74.2) | 35 (79.6) | 229 (73.4) | 1.00 | 1.00 |
| Prior SPTBs[b] | | | | | |
| Multiple (≥2) | 92 (25.8) | 8 (18.2) | 84 (26.9) | **0.47 (0.25–0.89)** | .58 (.25–1.31) |
| 1 | 264 (74.2) | 36 (81.8) | 228 (73.1) | 1.00 | 1.00 |
| Race | | | | | |
| Black race | 132 (37.1) | 16 (36.4) | 116 (37.2) | 0.96 (0.50–1.86) | .90 (.41–2.01) |
| Other | 224 (62.9) | 28 (63.6) | 196 (62.8) | 1.00 | 1.00 |
| Tobacco use[b] | | | | | |
| Yes | 70 (19.7) | 12 (27.3) | 58 (18.6) | 1.64 (0.79–3.38) | 1.88 (.90–3.96) |
| No | 286 (80.3) | 32 (72.7) | 254 (81.4) | 1.00 | 1.00 |

[a] Bolded results reflect statistically significant findings ($p < .05$).

[b] Model adjusted for maternal age, number of prior SPTB, and any tobacco use during pregnancy. All frequencies reflect column percentages.