International Journal of Gynecology and Obstetrics (2008) **103**, 144–148

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International Journal of GYNECOLOGY & OBSTETRICS

CLINICAL ARTICLE

Centile charts of cervical length between 18 and 32 weeks of gestation

Gerhard Theron [a,*], Christene Schabort [a], Karin Norman [a], Mary Thompson [b,c], Lut Geerts [a]

[a] *Department of Obstetrics and Gynecology, Tygerberg Hospital, Cape Town, South Africa*
[b] *Department of Biostatistics, University of Washington, Seattle, USA*
[c] *Biostatistics Unit, Medical Research Council, South Africa*

Received 10 March 2008; received in revised form 30 May 2008; accepted 2 June 2008

KEYWORDS
Centile chart;
Cervical length;
Longitudinal measurements;
Parity;
Ultrasound

Abstract

Objective: To establish a centile chart of cervical length between 18 and 32 weeks of gestation in a low-risk population of women. *Methods:* A prospective longitudinal cohort study of women with a low risk, singleton pregnancy using public healthcare facilities in Cape Town, South Africa. Transvaginal measurement of cervical length was performed between 16 and 32 weeks of gestation and used to construct centile charts. The distribution of cervical length was determined for gestational ages and was used to establish estimates of longitudinal percentiles. Centile charts were constructed for nulliparous and multiparous women together and separately. *Results:* Centile estimation was based on data from 344 women. Percentiles showed progressive cervical shortening with increasing gestational age. Averaged over the entire follow-up period, mean cervical length was 1.5 mm shorter in nulliparous women compared with multiparous women (95% CI, 0.4–2.6). *Conclusions:* Establishment of longitudinal reference values of cervical length in a low-risk population will contribute toward a better understanding of cervical length in women at risk for preterm labor.

1. Introduction

Annual perinatal statistics for 2006 from the Tygerberg Cape Metropole region, South Africa, showed that 23.2% of neonates had a low birth weight (LBW, 2500 g or less) and that the perinatal mortality rate was 78.5 per 1000 deliveries. The number of LBW neonates, which includes preterm neonates (delivered before 37 completed weeks of gestation), has remained relatively unchanged over the last 17 years [1]. A high rate of perinatal mortality is associated with low birth weight neonates [2], and several studies conducted in low-income countries have found a similar trend. Pattinson [3] found that spontaneous preterm

* Corresponding author. Department of Obstetrics and Gynecology, Faculty of Health Sciences, PO Box 19063, Tygerberg, 7505, South Africa. Tel.: +27 21 9389217; fax: +27 21 9322455.
E-mail address: gbth@sun.ac.za (G. Theron).

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doi:10.1016/j.ijgo.2008.06.011

labor was the primary obstetric cause of death in 17% of perinatal deaths in South Africa; and this corresponds with several studies conducted in other African countries and elsewhere [4–10].

In recent years, examination of the cervix and measurement of cervical length in particular has assumed an important role in the management and diagnosis of women with an increased risk for preterm labor. Certain findings allow clinicians to detect and sometimes alter the outcome of a pregnancy at risk for preterm labor [11]. The addition of transvaginal ultrasound has allowed clinicians to obtain a more accurate measurement of the cervical canal and the increased accuracy of this method has helped to identify women at an increased risk [12].

Hoesli et al. [13] highlighted the need for longitudinal charts of cervical length and cautioned against using a single cutoff value at a certain gestational age. In addition, they reasoned that cervical lengths differ in various populations and require development of population-specific charts.

The aim of the present study was to establish the distribution of cervical length measurements to construct centile charts for both nulliparous and multiparous women from a low-risk population in South Africa.

2. Materials and methods

The study was conducted between February 1, 2002 and November 7, 2003. Consecutive women using public healthcare facilities for their pregnancy care in the Cape Metropole region of South Africa, who booked at the Bishop Lavis prenatal clinic between 16 and 23 weeks of pregnancy, and who met the inclusion criteria were recruited to the study. Inclusion criteria were a singleton pregnancy with no pregnancy complications. Women who had two previous episodes of placental abruption, previous preterm labor before 34 weeks of pregnancy, previous midtrimester spontaneous abortion, previous early onset (before 34 weeks) severe pre-eclampsia, insulin-dependent diabetes mellitus, positive HIV status, or placenta previa in the current pregnancy were excluded from the study.

The community served by the Bishop Lavis clinic is predominantly of low socioeconomic status. The study was explained to the women and written informed consent was obtained. The study protocol was approved by the Committee for Human Research (Ethics Committee) of the Faculty of Health Sciences of Stellenbosch University.

The first cervical measurement coincided with the ultrasound scan performed between 16 and 23 weeks to determine gestational age. Measurements of biparietal diameter, head circumference, abdominal circumference, and femur length were used to obtain the average gestational age using Chitty reference ranges [14]. Transvaginal measurement of the cervix was carried out as described by Heath et al. [15] using a 5 MHz transducer (Toshiba Corporation) covered with a disposable sterile sheath. The first measurement was obtained between 16 and 23 weeks of gestation and the women were requested to return at 2-3 weekly intervals up until 32 weeks (16, 18, 20, 23, 26, 28, 30, 32). Women were reimbursed their traveling expenses for visits that did not coincide with routine visits.

When either the internal or external cervical os—the ultrasonic landmarks used for measuring cervical length—was not visible, the image was considered indistinct for accurate assessment. The true position of the internal os was defined as the proximal end of the endocervical mucosa, which lines the endocervical canal. Funneling was defined as dilatation at the level of the internal cervical os of 5 mm or more. Cervical length measurements associated with funneling or indistinct images were excluded. Ultrasound measurements were carried out by two qualified sonographers.

For the statistical analysis it was assumed that the distribution of cervical length at each gestational age could be characterized by 3 parameters: a power transformation to normality (L); location (M); and spread (S)—all assumed to change smoothly with gestational age [16]. Fractional polynomials (FPs) were used to model L, M, and S over gestational age [17]. FPs allow flexibility in shape and have the advantage over semiparametric or nonparametric approaches in that the corresponding percentiles of the fitted distributions can be readily expressed in closed functional form. FPs up to degree 2 based on powers from the set $P=\{-2, -1, -0.5, 0, 0.5, 1, 2, 3\}$ were considered. By a fractional polynomial of degree 2 in X (gestational age), we mean a linear combination of power transformations of the form: $\beta_0 + \beta_1 X^{p_1} + \beta_2 X^{p_2}$, where $X^{p_k} = \ln(X)$ if $p_k = 0$ and $X^{p_2} = X^p \ln(X)$ if $p_1 = p_2 = p$. In practice, it has been found that FPs of degrees higher than 2 are seldom required and may, on the contrary, introduce implausible structure into modeled relationships [17,18].

For each degree ($m = 1, 2$), the best-fitting FP model for M and then S was identified as that with the smallest residual sum of squares. The choice between best-fitting models of different degrees was based on an approximate χ^2 test with significance level set at 0.05. A fractional polynomial model was first identified for M. Next, an FP model for the regression on gestational age of the absolute residuals from the chosen model for M was similarly identified, to provide a model in gestational age for S. Using the identified FP model forms for M and S, maximum likelihood was then used to simultaneously estimate the coefficients of FP models for L, M, and S for each degree = 1 (FP1) model for L. The best FP1 model for L was compared with the null model (L independent of gestational age) using an approximate χ^2 test with significance level set at 0.05. The final FP coefficient estimates for L, M, and S were based on maximizing the associated likelihood. Standard errors were based on robust estimates of variance to accommodate the repeated measurements for each individual.

The fit of the longitudinal reference ranges was evaluated by comparison, at each gestational age, of the observed and expected frequencies within and beyond the percentile bounds and by examining the distribution of z scores, calculated for each observation based on the fitted parameters. Separate models for nulliparous and multiparous women were constructed and centile estimates for the 10th, 50th, and 90th centiles were derived. The 3rd and 5th centiles for all women (ignoring parity) were also estimated. All analyses were carried out using Stata Version 9.1 (Stata Corp, College Station, TX, USA).

3. Results

A total of 360 women were recruited over the study period; 9 women were lost to follow-up and 7 were iatrogenically delivered preterm because of complications, leaving 344 women for the analysis. The distribution of cervical length at each recorded gestational age excluded measurements that were associated with funneling (9 observations in 4 women) or observations where the image was indistinct (18 records

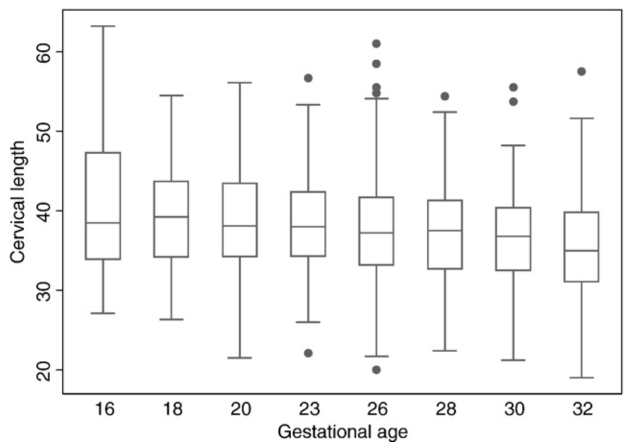

Figure 1 Longitudinal boxplots of observed cervical lengths over gestational age. The boxes extend from the 25th to the 75th percentile, with the horizontal line within the box showing the median. The length of the box is the interquartile range (IQR). The "whiskers" extend to the smallest (largest) observed value within 1.5 IQRs of the box. All values beyond the whiskers are regarded as outliers and are shown individually.

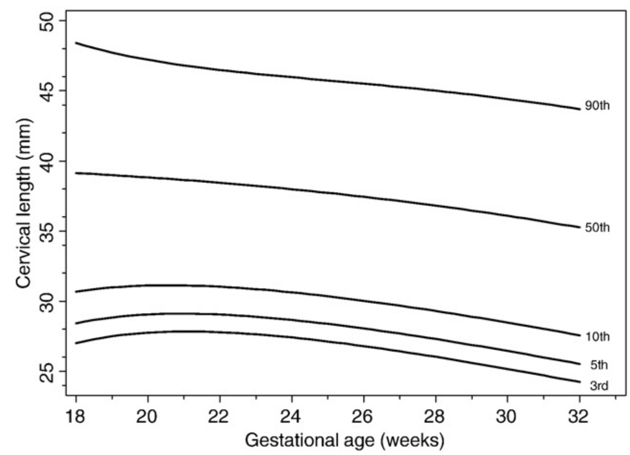

Figure 3 Estimated 3rd, 5th, 10th, 50th, and 90th percentiles of cervical length between 18 and 32 weeks of gestation for all women.

from 10 women). The mean first recorded gestational age was 22 weeks (range, 15–24 weeks). The frequency of cervical length measurements at different gestational ages was: 34 women at 16 weeks, 101 women at 18 weeks, 240 women at 20 weeks, 308 women at 23 weeks, 283 women at 26 weeks, 262 women at 28 weeks, 249 women at 30 weeks, and 233 women at 32 weeks (n = 1710 cervical length measurements). The median number of serial measurements taken from each individual was 5 (range, 1–8).

The mean age of the cohort was 23.2 years (range, 15–39 years), the median parity was 0 (range, 0–5), and the median gravidity was 2 (range, 1–7). The mean gestational age at delivery was 39.2 weeks (range, 23–45 weeks), and mean birth weight was 3021 g (range, 504–4520 g). Regarding gestational age at delivery, 2.6% of women delivered before 34 completed weeks of gestation and 9.9% delivered before 37 weeks.

The observed cervical lengths are summarized by gestational age in Fig. 1. We can see a decline with gestational age in the median and quartiles and some indication of asymmetry in the distributions. Fig. 2 shows the fitted probability distributions (based on FP modeling) of cervical length for nulliparous and multiparous women separately at 18 and 32 weeks of gestation. The study found that, averaged over the duration of follow-up, multiparous women had significantly longer cervices compared with nulliparous women ($P = 0.008$). On average, this difference was 1.5 mm (95% confidence interval, 0.4–2.6).

Centile charts of cervical length over gestational age as a reference for our population were estimated for all women (Fig. 3) and separately for nulliparous (n = 178) and multiparous women (n = 166 women) (Fig. 4). The percentile estimates and associated standard errors are shown in Table 1. Because of the relatively small number of women enrolled by week 16, we report results from week 18 onward, although measurements at all gestational ages were used in the estimation. The percentiles decrease with increasing gestational age. Note the lower precision of the estimated percentiles at low (week 18)

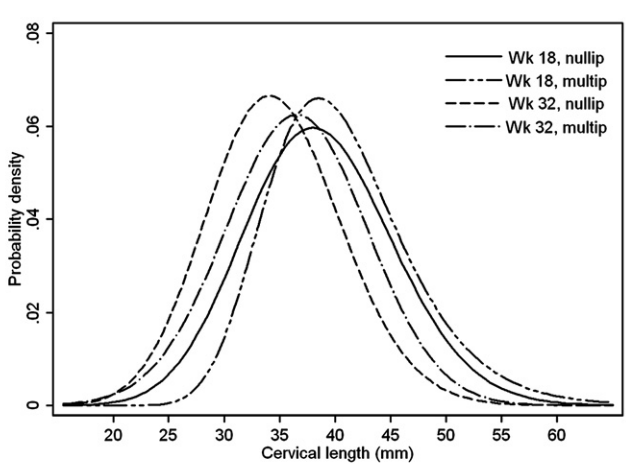

Figure 2 Fitted cervical length probability distributions for nulliparous and multiparous women at 18 and 32 weeks of gestation.

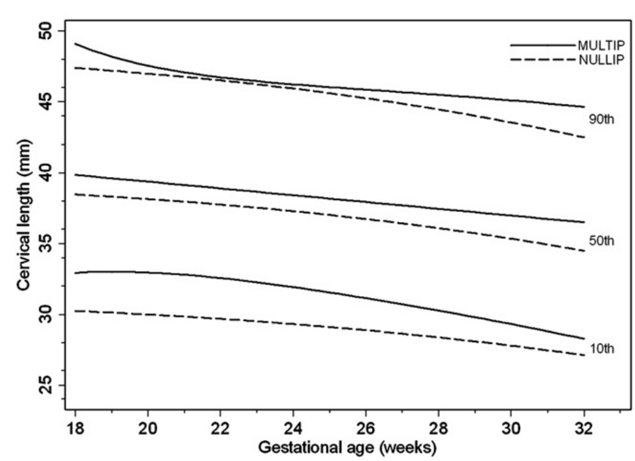

Figure 4 Estimated 10th, 50th, and 90th percentiles of cervical length between 18 and 32 weeks of gestation for nulliparous (broken line) and multiparous women (solid line).

Table 1 Cervical length: 3rd, 5th, 10th, 50th, and 90th percentile estimates and standard errors for all women and 10th, 50th, and 90th percentile estimates and standard errors for nulliparous and multiparous women

	All women				
Week	3rd	5th	10th	50th	90th
18	27.0 (0.52)	28.4 (0.46)	30.9 (0.40)	39.1 (0.34)	48.4 (0.59)
20	27.7 (0.43)	29.1 (0.39)	31.1 (0.34)	38.8 (0.32)	47.2 (0.46)
22	27.8 (0.42)	29.0 (0.38)	31.0 (0.34)	38.4 (0.31)	46.5 (0.42)
24	27.4 (0.41)	28.7 (0.37)	30.6 (0.33)	38.0 (0.30)	46.0 (0.39)
26	26.8 (0.40)	28.1 (0.37)	30.0 (0.33)	37.4 (0.30)	45.5 (0.38)
28	26.0 (0.42)	27.3 (0.39)	29.3 (0.36)	36.8 (0.31)	45.0 (0.41)
30	25.2 (0.47)	26.4 (0.44)	28.5 (0.41)	36.1 (0.36)	44.4 (0.47)
32	24.2 (0.54)	25.5 (0.51)	27.6 (0.48)	35.2 (0.42)	43.7 (0.57)

	Nulliparas			Multiparas		
Week	10th	50th	90th	10th	50th	90th
18	30.2 (0.49)	38.5 (0.51)	47.4 (0.64)	32.9 (0.49)	39.8 (0.53)	49.1 (0.93)
20	30.0 (0.47)	38.1 (0.48)	47.0 (0.60)	33.0 (0.40)	39.4 (0.47)	47.6 (0.74)
22	29.7 (0.45)	37.8 (0.45)	46.5 (0.56)	32.6 (0.40)	38.9 (0.44)	46.7 (0.67)
24	29.3 (0.44)	37.3 (0.42)	45.9 (0.52)	31.9 (0.40)	38.4 (0.42)	46.2 (0.60)
26	28.9 (0.43)	36.7 (0.41)	45.3 (0.50)	31.1 (0.43)	37.9 (0.43)	45.9 (0.57)
28	28.4 (0.45)	36.1 (0.43)	44.5 (0.51)	30.3 (0.48)	37.4 (0.47)	45.5 (0.60)
30	27.8 (0.48)	35.3 (0.48)	43.5 (0.57)	29.3 (0.55)	37.0 (0.53)	45.1 (0.67)
32	27.1 (0.55)	34.5 (0.57)	42.4 (0.68)	28.3 (0.66)	36.5 (0.60)	44.6 (0.77)

and higher (weeks 30 and 32) gestational ages and when the samples are stratified according to parity.

4. Discussion

Centile charts of cervical length were constructed for a population of women with singleton pregnancies. In addition to being from a low socioeconomic group, the study population did not include women with specific risk factors for preterm labor or delivery. Women with insulin-dependent diabetes mellitus present at time of recruitment were also excluded because of the known risks associated with these pregnancies. HIV positive women were excluded because the assumption, at the time of the study, was that these women are at increased risk for preterm labor; this assumption has subsequently been proven correct [19]. All cervical length observations used to construct these charts were made by two experienced observers.

In this low-risk study population, parity was considered to be the main variable that might influence cervical length. The results confirm the finding of Iams et al. [20] that multiparous women had significantly longer cervices compared with nulliparous women. In the present study the mean difference was 1.5 mm and this corresponds with the results of Iams et al. [20] who found a difference of 1.9 mm. Although the difference in length is small, it is an interesting finding that is contrary to clinicians' general perception. Progressive cervical shortening occurs between 18 and 32 weeks, as seen in several other studies [21]. This is biologically understandable, but emphasizes the relevance of identifying an unusually short cervix at an early gestational age. The slightly longer cervices found in the present study compared with Iams et al. [20] support the argument of Hoesli et al. [13] that cervical lengths differ in different populations, and require population-specific charts.

Although separate centile charts were developed for nulliparous and multiparous women, in clinical practice a single chart will be more user friendly, especially when printed copies are needed in a setting with limited resources. With automated ultrasound equipment, separate charts according to parity could easily be stored in the database. Once information regarding parity has been entered, the correct centile chart will automatically be selected. However, it should be noted that the sample sizes for these separate charts were modest and hence the accompanying standard errors of the percentile estimates are larger than for the pooled chart.

Despite the vast amount of research into the causes and prevention of preterm labor, there has been no impact on the overall rate of preterm delivery worldwide. This remains a global dilemma for both high- and low-income countries, with women in low-income countries at an even higher risk for delivering preterm neonates. Current attempts to help prevent preterm labor have generated disappointing results, and have had little impact on the rate of preterm birth. This is due to a combination of the poor positive predictive value of the screening tests currently available as well as a lack of interventions available to treat the problem.

Establishment of longitudinal reference values of cervical length for a low-risk population will contribute toward a better understanding of cervical length in women at risk for preterm labor. Further studies are required to establish the sensitivity, specificity, and predictive values of cervical length for women at both low- and high-risk for preterm labor.

Acknowledgments

The study was supported by funding from the University of Stellenbosch and a grant from the Harry Crossley fund.

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