

# Correlation between Endocervical Length in the First Trimester and Spontaneous Preterm Delivery

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## Abstract

**Introduction:** Prematurity is a public health problem in Brazil, with 12% of deliveries occurring before 37 weeks of gestation. The measurement of the cervix in the second trimester is already established as a method of screening for prematurity and some studies point out advantages to start this screening in the first trimester. **Objective:** To define the correlation between the length of the endocervix by transvaginal ultrasound in the first trimester (11 to 14 weeks) with spontaneous early deliveries. **Method:** A prospective and observational study realized in a suplementar and private ultrasound clinic and hospital of Porto Alegre, Brazil between 2019-2020. Ultrasound screening of cervix was performed in singleton pregnancies in first and second trimester of pregnancy and correlated with age of delivery. **Results:** 142 pregnant women were studied, 80% were in the first pregnancy. The average age was 33.8 years. The rate of prematurity was 18% before 37 weeks and 4% before 34 weeks. The average of cervix measured in the first and second trimesters in deliveries before 34 weeks was 32.7 mm and 29.3 mm, respectively. In term deliveries the median cervical length was 38.8 mm and 37.8 mm, respectively. When analyzing the measurements of the cervix in the second trimester, the cervix was smaller ( $p = 0.008$ ) among deliveries below 34 weeks (29 mm) than deliveries after 37 weeks. No statistically related differences were found between preterm birth and first trimester cervix measurements. **Conclusions:** In this study, we did not observe a statistically significant relationship between first trimester cervix measurement and prematurity. More studies are needed to

evaluate this finding. However, the measurement of the cervix in the second trimester is different from that found in the literature. This suggests a possible new cut-off point that increases the sensitivity of transvaginal ultrasound as a method of preventing prematurity.

## Keywords

Preterm Birth, Screening, Cervical Length Measurement, Preterm Birth Prevention Clinic

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## 1. Introduction

Prematurity is still the cause of the highest neonatal mortality and morbidity, even in developed countries, we observe rates between 5% to 15% of early deliveries. In Brazil, the incidence of premature births is approximately 12% [1]. The finding of a short cervix in pregnancy is a risk factor for preterm delivery and the search for a method for screening can be an effective strategy in the search for prevention [2]. The measurement of endocervical length by transvaginal ultrasound between 19 to 23 weeks of gestation is already established as a universal screening method and some studies have already shown advantages to start this screening in the first trimester, between 11 to 14 weeks [3] [4].

According to some studies, there was an important decrease in the length of the cervix between the first and the second trimester in pregnant women who had a premature birth [5].

This study aims to assess whether the measurement of the cervix, assessed by transvaginal ultrasound, in the first trimester is related to preterm spontaneous delivery and its correlation with the measurement in the second trimester.

## 2. Method

Prospective study carried out between 2019 and 2020 in a private clinic in Porto Alegre, Brazil. All births took place in a private hospital in Porto Alegre.

The transvaginal scan measures the length of the cervix in the first trimester, between 11 to 13 weeks and 6 days. The second measurement was performed in the morphological exam of the second trimester, between 20 to 23 weeks and 6 days. Pregnant women with fetal malformations, multiple pregnancies and a history of cervical surgeries such as conization, amputation and cerclage or who had their birth in another institution were excluded.

### 2.1. Diagnosis of Premature Birth

Premature birth is defined as the occurrence of birth before 37 complete weeks of gestation. According to the WHO (World Health Organization), prematurity is classified as: extreme, when it occurs in births before 28 weeks; early below 34 weeks and late between 34 and 37 weeks [6].

Regarding the outcome, this classification was taken into account and three

groups were formed. The outcome of pregnancy was correlated with the length measurement in the first and second cervical length assessment.

## 2.2. Technique for Cervical Measurement

The measurement of the uterine cervix should ideally be performed by ultrasound (USG) via transvaginal (TV) as it allows the visualization of its entire length, from the internal portion to the external cervical hole. The difficulty in measuring the cervix in the first trimester is the differentiation between the lower segment of the uterus and the internal orifice of the cervix. The method has a low cost and good reproducibility [7]. It is important that examiners are certified by the Fetal Medicine Foundation (FMF). In this study, measurements were taken by two doctors, both certified by the reference institution. The ultrasound scanners who performed the ultrasound were certified by the FMF and used the standard technique recommended by the institution.

During the exam, women were instructed to proceed with bladder emptying. The transducer is inserted in the middle third of the vagina, approximately 3 cm from the cervix, so that minimal pressure is exerted so as not to distort position or shape. Then we obtain an image of the cervix in sagittal section, with visualization of the entire cervical length, including the internal cervical orifice, the echogenic mucosa and the external cervical orifice. When the sagittal cut is obtained, the image is magnified until it occupies approximately 75% of the screen, the calipers being positioned on the anechogenic endocervical line in order to measure the distance between the internal and external orifices. Three measures must be taken, the smallest measure being considered among them. There should be a 2 to 3 minute interval between measurements, as recommended by the Fetal Medicine Foundation, as in 1% of cases there may be a change in the measure due to sporadic contractions. The smallest measure should be considered. Obeying these criteria, the measurement of cervical length is a highly reproducible method and in 95% of cases the difference in measurements between two observed does not exceed 4 mm [8].

## 2.3. Statistical Analysis

Data was entered into the Excel program and later exported to the IBM SPSS version 20.0 program for statistical analysis. The normality of quantitative variables was assessed using the Kolmogorov Smirnov test. Quantitative variables with normal distribution were described by the mean and standard deviation and those with asymmetric distribution by the median and the interquartile range (25th and 75th percentiles). Quantitative variables with normal distribution were compared between two categories by Student's t test for independent samples and between times by Student's t test for paired samples. Categorical variables were described by frequencies and percentages and associated using Fisher's exact test. A significance level of 5% was considered for the established comparisons.

Calculate the sample size for correlation between the two measurements in order to estimate as statistically significant a correlation coefficient between cer-

vical measurements of 0.30, a power of 90% and an  $\alpha = 0.05$ , 113 participants are needed. This calculation was performed with the WINPEPI 11.65 program (Abramson, J.H. WINPEPI updated: computer programs for epidemiologists, and their teaching potential. *Epidemiologic Perspectives & Innovations* 2011, 8: 1).

## 2.4. Ethical Aspects

This research was initiated after approval by the Research Ethics Committee of Hospital Moinhos de Vento in Porto Alegre, RS/Brazil. All research protocols were submitted and approved in the CEP/CONEP System through the Brazil Platform (CAAE 14838319.40000.5330).

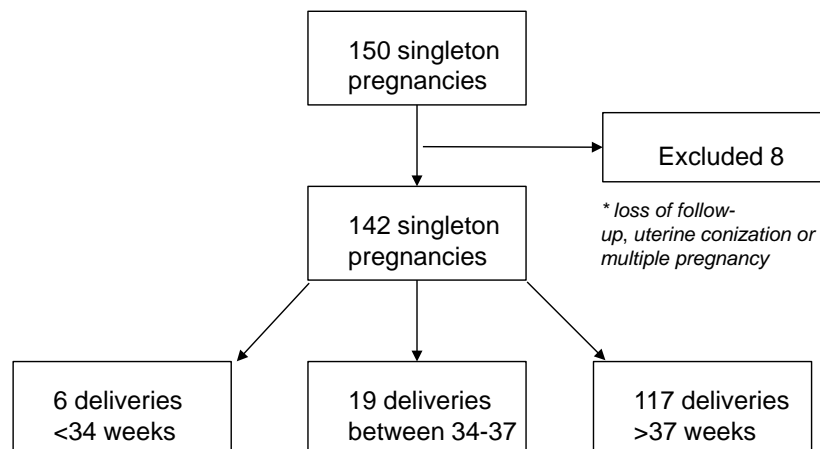
The examinations were carried out at the clinic at no additional cost to the participants or to the health plan, after signing the informed consent form. In the second stage of data collection, the medical records were analyzed at the Hospital Moinhos de Vento.

## 3. Results

During the study period we measured the cervical length in 150 singleton pregnancies. We excluded 8 cases (loss of follow-up, uterine conization or multiple pregnancy). In 142 cases included the median age was 33.8 ( $\pm 4.3$ ) years and 80% were in their first pregnancy (**Figure 1**). Comorbidities were found in 17% of the participants, the most common gestational diabetes and hypothyroidism (**Table 1**). The average gestational age at birth was 38 weeks. Of the 142 pregnancies, 25 (18%) progressed to delivery before 37 weeks: 6 deliveries before 34 weeks, one of them before 28 weeks, and 19 deliveries between 34 to 37 weeks (**Table 1**).

Analyzing the 142 women, we divided them into 3 groups. The first group is births with gestational age < 34 weeks. The average cervical length in the first trimester 32.7 mm and in the second trimester 29.3 mm ( $p = 0.461$ ) (**Figure 2**).

In the second group (births between 34 to 37 weeks), we found average measurements of cervical length 38.2 and 38.8 mm in the first and second trimesters, respectively ( $p = 0.658$ ).



**Figure 1.** Flowchart.

**Table 1.** Maternal characteristics and obstetric history in the screened population.

Characteristics	Categorical variables n (%)
Maternal age, in years	33.8 ± 4.3
obstetric history, number of pregnancies, n (%)	
1 pregnancy	80 (62.0)
2 pregnancies	30 (23.3)
3 or more	19 (14.7)
Previous deliveries, n (%)	
None	135 (94.6)
1 or more	7 (5.4)
Cesarean, n (%)	
None	104 (80.6)
1 or more	25 (19.4)
Miscarriage, n (%)	
None	105 (81.4)
1 or more	24 (18.6)
Diabetes Mellitus, n (%)	17 (12.0)
Hypothyroidism, n (%)	7 (4.9)
Gestational age (IQR)	38 (37 - 39)
Deliverie's gestational age, n (%)	
<34	6 (4.2)
34 - 37	19 (13.4)
≥37	117 (82.4)
Delivery, n (%)	
Cesarean	112 (86.0)
Vaginal	30 (14.0)

SD: standard deviation; IIQ: interquartile range. There is missing data.

In the group of deliveries after 37 weeks, the average cervical length was 38.8 mm in the first trimester and 37.8 mm in the second trimester ( $p = 0.056$ ) (**Table 2**).

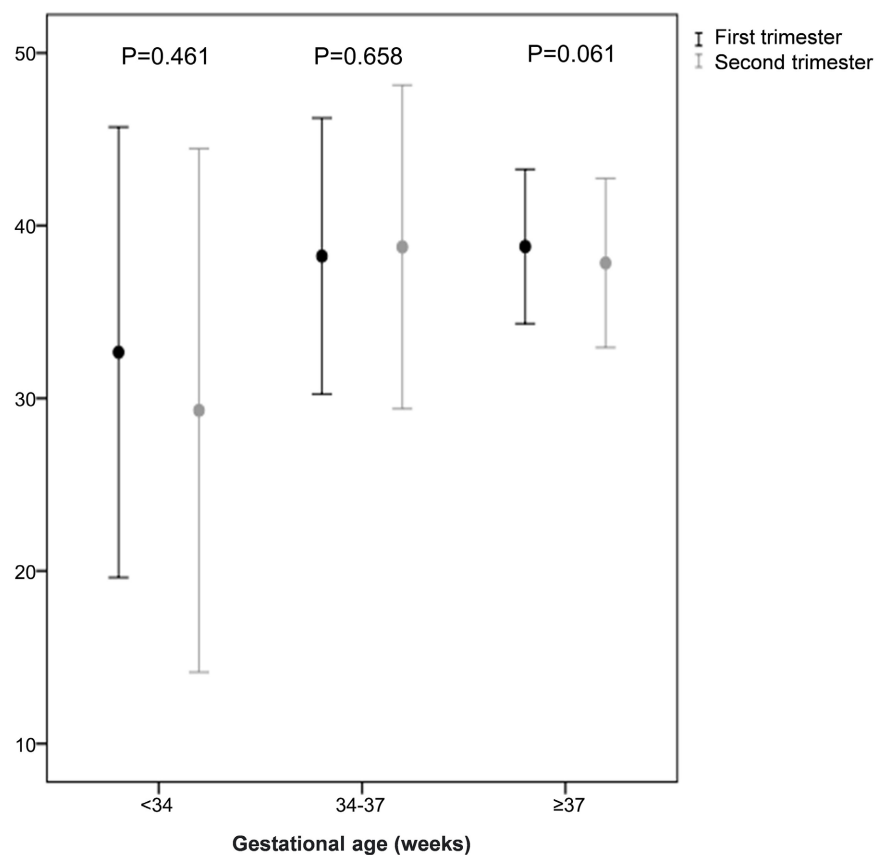
In the assessment of the first trimester, when comparing deliveries before 34 weeks and those after than 37 weeks, the measurement of the cervix was 32.7 and 38.8 mm, respectively ( $p = 0.059$ ). When analyzing the measurements of the cervix in the second trimester, the average measurement was 29,3 mm in deliveries before 34 weeks while in deliveries above 37 weeks the average measurement was 37.8 mm ( $p = 0.008$ ) (**Table 2**).

The measurement below 25 mm in the second trimester was found in 5% of the 142 pregnant women. Pregnant women with a cervical measurement in the

**Table 2.** Comparison of cervical measurements in the first and second trimester according to gestational age at birth.

	General median	<34 w n = 6	34 - 37 w n = 19	≥37 w n = 117	P entre faixas de idade
Cervical Length					
First trimester	36.5 ± 8.5	32.7 ± 13.0	38.2 ± 8.0	38.8 ± 4.5	0.056
Second trimester	35.3 ± 9.6	29.3 ± 15.2 <sup>a</sup>	38.8 ± 9.4 <sup>b</sup>	37.8 ± 4.9 <sup>b</sup>	<b>0.008</b>
P between trimesters		0.461	0.658	0.061	

Data presented by the mean ± standard deviation; compared between quarters by Student's t test for paired samples and between gestational age ranges by ANOVA. a, b: different letters mean statistically different means.

**Figure 2.** Comparison of cervical measurements in the first and second trimester according to gestational age at birth.

second trimester below 25 mm had an average cervical measurement at the first trimester of 27.7 mm and those with a second trimester measurement above 25 mm had an average of 39.0 mm at the first moment.

In this group, only one participant did not receive any type of intervention and evolved to extreme prematurity. All other participants received interventions to prevent prematurity: vaginal progesterone 200 mcg/day, half of them association of progesterone + Arabin cervical pessary and one of them progesterone.

rone + elective cerclage. The interventions were performed by the patients' assistant physicians. No single protocol of intervention was defined for this study.

#### 4. Discussion

The rate of prematurity found in this study was 18%, higher than the average rate in Brazil, which is approximately 12%, according to studies carried out in low-risk populations, in reference maternity hospitals in Brazil [9]. These studies were performed in women attending in the public health system, whereas our study was in supplementary health systems, where maternal characteristics can be different in our country. The data recorded in 27 Brazilian public maternity hospitals, the maternal age of most births is of young women, below 34 years old, 59% are non-white and 66% had a low level of education [9].

Spontaneous premature births correspond to approximately 75% of cases of prematurity and its etiology is a multifactorial process [10]. Maternal factors associated with a higher risk of spontaneous premature birth include advanced maternal age, factors related to maternal lifestyle such as stress, overwork and physical effort or standing for long periods, smoking and excessive alcohol consumption [11]. Extreme prematurity was found in 1% of patients, compatible with data in the literature, which shows 1.8% of extreme prematurity, in patients who also did not receive interventions [5].

In our study, the length of the uterine cervix assessed by transvaginal ultrasound in the first trimester shows a tendency to be related to lower cervix measurements in the second trimester and with births below 34 weeks. However, in this study, we did not find statistical significance for this relationship. Study by Carvalho *et al.* demonstrated that there is no difference in the measurement of the cervix between patients in the first trimester in relation to prematurity, but there is an important decrease in the length of the cervix between the first and the second trimester in patients who presented prematurity [5]. Despite attempts to assess whether progressive cervical shortening is a predictor of prematurity, it was not significantly superior to the single measurement performed in the second trimester and is more cost-effective. In this sense, screening with repeated cervical measurements is not recommended as a way of identifying the risk of prematurity [12].

Though, some studies found in the literature demonstrate that short necks in the first trimester are associated with earlier births [5]. Zalar *et al.* classifies the measure of the cervix in percentiles and notes that the cervix below 40 mm, in the first trimester, which would be the 10th percentile, would be related to the increased risk for childbirth with gestational age below 30 weeks [13]. This data is similar to that found in our study, where the average measurement of the cervix of 32 mm was found between births below 34 weeks, and may be an ally in the identification of the group of pregnant women at risk for birth below 34 weeks.

From the data analyzed, it was observed that those with a second neck mea-

surement below 25 mm had an average neck measurement at the first moment of 27.7 mm. These data suggest that a borderline measure in the first trimester should warn of the risk of prematurity and perhaps the cutoff point in the first trimester will be different from the second trimester [5].

There is no consensus on the monitoring of the cervical measurement, even for high-risk pregnant women, but there is a recommendation that pregnant women with premature birth prior to the cervical measurement should be evaluated every 2 weeks between 14 and 24 weeks [8]. So far, this routine has not been adopted in most Brazilian services.

Another important data seen in the study is that the average measurement of cervix in second trimester was 29.3 mm in deliveries before 34 weeks. Thus, it is discussed whether the cutoff point for measuring of the cervix associated with prematurity is between 25 and 30 mm and not 25 mm, as we use today. This could increase the sensitivity of the test without decreasing specificity. More studies are needed to show the same relationship.

The measurement of the cervix in the second trimester is already recommended by the International Federation of Gynecology and Obstetrics (FIGO) and by the Brazilian Federation of Gynecology and Obstetrics (FEBRASGO), as long as you have the opportunity to perform it together with morphological ultrasound. But with the progress of the studies, and the results that have been found, the measure in the first trimester may be an opportunity for early screening of a subgroup of high risk of prematurity.

It is important to highlight that the pregnant women who underwent interventions had late premature births, after 34 weeks. Of the measures adopted for prevention, once the risk was identified by the measurement of the cervix, the most performed was the prescription of progesterone, which led to a 39% reduction in births below 34 weeks. This data is similar to that found in the literature, which shows a 40% reduction in premature births in women with a single pregnancy, with no previous history of premature birth and short neck ultrasound finding [14].

Ideally, comparisons of measures in the first and second trimesters should be for women who have not undergone interventions, which was not possible in this study, since the vast majority received progesterone or pessaries to prevent prematurity. These measures taken may have interfered with the result of the second trimester exam. It is possible that the identification of a borderline neck, associated with risk factors and preventive measures, influenced the outcome, since we observed a decrease in the average length of the uterine cervix from the first to the second exam, as described in the literature [15].

Another measure observed in our study was the placement of a cervical pessary, a non-invasive and simple technique that supports the cervix. Pregnant women who used the method also used progesterone, making it difficult to analyze the measure in isolation. In a review of the Cochrane Library, we found a randomized controlled trial, which included 385 pregnant women with a neck



smaller than 25 mm between 18 and 22 weeks of pregnancy. The pessary was used in 192 women, with a significant reduction in the incidence of spontaneous preterm delivery below 37 weeks, when expecting conduct [16].

The sensitivity of the method is greater in single pregnancies, asymptomatic and with risk factors (previous preterm delivery, cervical surgeries, Mullerian anomalies) [5] and should be considered, mainly, in these cases. The realization of a protocol to perform the measurement of the cervix in the first trimester may be an option considered to prevent prematurity, however it is necessary to evaluate a larger number of participants, preferably in a multicenter study, to establish the correlation of the measurement and the risk for preterm delivery.

Some limitations of this study must be considered. The population studied is a selected sample, with access to private medical care. Data may not replicate in other populations. Another limitation may be the sample size of the study, which may be the reason that there is no statistically significant relationship for the primary outcome.

## 5. Conclusion

The measurement of cervix performed in the first trimester is related to smaller measurements in the second trimester and with premature births. From this study, it was noted that the measure of 29 mm in the second trimester was associated with premature births. This leads to the discussion of defining new cutoff points for the measurement of the cervix, in order to increase the sensitivity of transvaginal ultrasound as a method of preventing prematurity. More studies are needed to show relationship of first trimester measures and prematurity.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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