Chapter

# Cervical Length and Perinatal Outcome

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## Abstract

Prematurity nowadays has taken on significant dimensions. It is a complex medical issue with socio-economic consequences. The estimation of cervical length, assessed during the second trimester of pregnancy, using transvaginal ultrasound, may help to reduce rates of prematurity. By predicting the risk of preterm birth and identifying women who are at high risk of preterm birth, certain practices could be implemented, such as the use of progesterone or cerclage placement. Nonetheless, it remains unsolved the question of certain strategies, such as the use of progesterone in pregnant women with shortened cervical lengths. This work examines the relationship of cervical length during pregnancy to the perinatal outcome.

**Keywords:** cervical length, cervical cerclage, Arabin pessary, perinatal outcome, cervical funneling, medical treatment

## 1. Introduction

Prematurity is defined as labor before the completion of 37 weeks of gestation is globally a major factor in infants' morbidity and mortality. It has been estimated that annually almost 15 million premature infants are born, consisting of about 11% of all the laborers globally. 85% of these cases are infants that have completed 32–36 weeks of gestation, 10% are infants that have completed 28–31 weeks of gestation and 5% are infants that are extremely premature which means the ones who do not have completed 28 weeks of gestation [1–4]. Prematurity seems not only to result in 1.000.000 deaths annually but also to be the leading cause of infants' death. The percentage of morbidity related to prematurity is also high, as huge as the number of financial resources that must be spent in this public health sector [1–4].

The most important risk factor of prematurity is the existence of an obstetric history of prematurity. Nonetheless, the prediction of premature birth is not an easy task due to its complexity. Various well-known risk factors for preterm birth in singleton

pregnancies have emerged from many studies. Among other risk factors of prematurity are also multiple pregnancies [1–4].

What is more, the ultrasonographic estimation of cervical length before 24 weeks of gestation in singleton pregnancies is implemented during the second trimester of pregnancy. Studies show the inverse relationship between cervical length and preterm delivery, and since cervical length ultrasound assessment is a safe, reliable, and repeatable method, its use has been established in the second trimester of pregnancy aiming the detection of pregnancies at increased risk for premature birth and to the implementation of secondary prevention practices, which will be discussed later in this text. It has been estimated that women in triplet pregnancy with a cervical length < 25 mm between 15 and 24 weeks of gestation have a 51% risk of preterm delivery before the 32nd week of gestation. While in women that are at low risk of preterm birth and with the estimated risk of preterm birth in this population to be 4% (singleton pregnancies, absence of history of preterm birth in previous pregnancy), a correlation appears to exist between preterm birth and cervical length, measured by ultrasound between 19th and 24th week of pregnancy. In these singleton low-risk pregnancies it has been found that a cervical length of 15 mm occupies the third percentile, having a sensitivity of 8.2% and a specificity of 99.7% in the prediction of preterm birth below 32 weeks of gestation, with a cervical length of 25 mm corresponding to the tenth percentile in pregnancies of 16–24 weeks of gestation (threshold below which the cervix is described as "short") [5–10].

Furthermore, the risk of preterm birth appears to be higher when the detection of short cervical length occurs earlier in pregnancy. In addition, it is particularly interesting that the presence of a short cervix may somehow be added to other risk factors for preterm birth. For example, the combination of obstetric history of preterm birth and short cervix has a relative risk for preterm birth of 3.3, higher than the one that appears in pregnancies in which there is only a short cervix. Thus, it has been suggested by various organizations, such as ACOG, for women with a history of preterm birth to have their cervical length measured from the 16th to 24th week of pregnancy, while the question of whether it is worth applying the same practice to low-risk women is still controversial. The latter view is based on various studies suggesting that only a small proportion of low-risk, based on obstetric history, pregnant women will be able to be identified by ultrasound assessment of their cervical length (from the 5% of the primiparous women that eventually will give birth prematurely, only 23.3% of them have a short cervix in mid-pregnancy ultrasound). Another study found that although women with a cervix <25 mm give birth prematurely more frequently than women with cervical length > 25 mm calculated at mid-pregnancy, the vast majority of women with premature labor (82%) do not show a short cervix in the second trimester of pregnancy. Given the association between this cervical length in the second trimester of pregnancy and the risk of preterm birth, various medical practices have been proposed and studied, which are also applied in everyday clinical practice to prevent premature birth. The use of progesterone, cervical pessaries, and cervical cerclage each individually or all in combination used to treat "short" cervix, especially in singleton pregnancies, has raised many questions about the usefulness of these practices as measures to treat premature birth and also about the effectiveness of the above-mentioned treatment options [10–15].

Progesterone, the most researched and well-known technique of preterm birth prevention, can be administered in singleton pregnancies with a history of preterm delivery between 16 and 36 weeks of gestation at a dosage of 250 mg once weekly (17-OHPC), 200–400 mg orally, or 100–200 mg vaginally daily [10–15]. Studies have

shown that administering progesterone via intravaginal or intramuscular injections of 17-hydroxyprogesterone from the second trimester of pregnancy through the third significantly lowers the risk of preterm birth in women with "short" cervixes, whether or not they have a prior history of preterm birth. However, as far as high-risk women are concerned, there are studies, such as OPPTIMUM (multicenter, double-blind randomized study) that based on their data there is no statistically significant reduction in the risk of preterm delivery with intravaginal progesterone administration. Therefore, more evidence is expected in this field to demonstrate the benefit of progesterone to each group of women and the most effective route of its administration [10–15].

The aim of this study was to collect information on the deduction of results concerning the relationship between cervical length and perinatal outcome. Although cervical length during the second trimester of pregnancy can be a helpful tool for identifying women who have a high risk of preterm birth, the current study concentrated on the cervical length, estimated by ultrasound between 20 and 22 weeks of gestation, and the risk of preterm birth in singleton pregnancies. Moreover, the present study was not only limited to singleton low or high-risk pregnancies for preterm birth but also included data concerning the relationship between cervical length and risk of preterm birth in twin and triplet pregnancies.

What is more, this study tried to examine the importance of cervical length measurement in the first trimester of pregnancy in the estimation of preterm birth risk. Such a relationship could be really useful since this would allow earlier medical intervention for the prevention of preterm birth.

Also, this study presented the relationship between cervical length in the third trimester of pregnancy and perinatal outcome (time of spontaneous onset of labor, success rates of labor induction). Those all are matters that highly concern obstetricians nowadays [10–15].

Generally, the aim of this study was through the review of the literature, the recognition of the women who are at high risk for preterm birth, and the implementation of strategies that could eventually prevent preterm birth.

## 2. Method

The search was made through Medline, Pubmed, EMBASE, and Cochrane Library using as keywords the following expressions: transvaginal ultrasound in pregnancy, transvaginal evaluation of cervix during pregnancy, mid-trimester evaluation of the cervical length, cervical length and prematurity, cervical assessment in twin pregnancy, cervical evaluation in triplet pregnancies, cervical length in the first trimester of pregnancy. The studies that were used in the present study examined the relationship between cervical length in the first, second, and third trimesters of singleton, twin, and triplet pregnancies and the risk of preterm birth.

The next step was to categorize all the relative studies that were gathered, based on some common characteristics of each subgroup study population. So, the following subcategories of studies were created: cervical length during the second trimester of singleton pregnancies and risk of prematurity. Cervical length during the first trimester-early second trimester of pregnancy and correlation with mid-trimester cervical length and risk of prematurity. Cervical length during the third trimester of pregnancy and prediction of spontaneous onset of labor, prediction of the risk of caesarian section, and success rates of labor induction. All the studies that were related to one of these subcategories were examined further.

## 3. Results and discussion

Preterm birth, or the delivery of infants before 37 weeks of gestation, is a major contributor to neonatal morbidity and mortality and is therefore a problem with socioeconomic implications. It has been estimated that about 41,000 premature babies are born every day worldwide. Morbidity and mortality rates resulting from preterm birth are higher for "early" preterm infants (<28 weeks) and moderate preterm infants (28–32 weeks) and lower for "late" preterm infants (33–36 weeks). Since prematurity is associated with the appearance of various short- and long-term complications in neonates, such as retinopathy, cerebral hemorrhage, necrotizing enterocolitis, respiratory distress syndrome, neurodevelopmental disorders, one can easily understand the dimensions of this medical topic of prematurity [16–20].

Mortality rates appear to reach 44% for neonates 23 weeks old, 32% for 24 weeks old neonates, 12% for 25 weeks old neonates, 11% for 26 weeks old neonates, 8% for 27 weeks old neonates, and 2% for 28 weeks old neonates. The causes of death in preterm infants can be sometimes not clear and in each case, it is unclear which specific factor ultimately led to premature death. Often, neonates that end up in intensive care units for premature neonates have no other recognized cause of death than that of the general title of preterm delivery [16–20].

In Canada, these percentages have been translated into real costs and money that have to be spent in this sector of health. Specifically, the two-year survival rate was found to be 56% for "early" preterm infants, 92.8% for "moderate" preterm infants, and 98.4% for "late" preterm infants. Also, the mean hospitalization time for moderately preterm infants varied from 1.6 days at the age of 2 years to 0.09 days at the age of 10 years. The cost per neonate for the first 10 years of their life resulting from the above data is estimated to be $ 67,467 for an "early" preterm neonate, $ 52,769 for a moderate preterm neonate, and $ 10,010 for a "late" preterm neonate. So, the national amounts, if we take into consideration the above costs, would be $ 123.3 million for "early" preterm infants, $ 255.6 million for moderately preterm infants, $ 208.2 million for "late" preterm neonates, and $ 587.1 million for all the newborns. So, based on the above medical and financial data, the importance of finding and adopting early prevention programs is fully understandable [16–20].

This can theoretically be achieved through the application of programs of cervical length measurement in the second trimester of pregnancy and its association with the risk of preterm labor. Such programs aim to identify and characterize women as high risk, in which "short" cervical length in combination with other characteristics from women's obstetric history will lead to the subsequent implementation of practices that will prevent preterm birth, leading to a significant reduction in prematurity rates.

Transvaginal ultrasound examinations of the cervical length have been shown to accurately predict preterm labor in both asymptomatic low-risk women and those who are already showing signs of preterm labor. Also, several studies have examined the use of transvaginal ultrasonography in high-risk asymptomatic women with significant differences to be noted between these studies regarding the cervical length that is considered as pathological, pregnancy age at which the measurement should be performed, and the gestational age that preterm labor eventually happens.

Several meta-analyses have examined the association between transvaginally measured cervical length and the prediction of preterm birth in asymptomatic women with singleton or multiple pregnancies. A systematic review of Crane, which included a sample of 2258 high-risk asymptomatic women with singleton

pregnancies, concluded that there was an inverse relationship between cervical length and the possibility of preterm labor. The cervical threshold under which the cervix was considered to be short was set at 25 mm, predicting with high sensitivity the risk of premature birth below 35 weeks of gestation, while women with a prior history of preterm labor and cervical surgery were identified as high risk for preterm labor. It was also found that the likelihood of preterm birth below 35 weeks is less in cases where cervical length < 25 mm is measured at 20–24 weeks of gestation, than the likelihood of preterm labor in cases where cervical length < 25 mm is measured at a gestational age less than 20 weeks or more than 24 weeks [20–24].

The women with a history of automatic onset of preterm birth included in the above analysis did not differ from those women who were getting into premature labor after premature rupture of fetal membranes and automatic onset of rhythmic contractions. And since the pathogenetic mechanisms in these two broad categories of preterm birth differ significantly, the predictive value of transvaginally measured cervical length was examined separately in these two subgroups. Some of the studies used in this analysis included a variety of risk factors for preterm birth, such as maternal age and smoking. These risk factors did not appear to have the same predictive value as other risk factors, such as history of previous preterm birth and presence of abnormalities in the uterus, so a subsequent statistical analysis was performed in this study and found that the results of the analysis were still the same even after exclusion of Watson's study that included smoking in older women in risk factors [24–28].

Previous studies have also noted the association between cervical surgeries and preterm labor. In Crane's meta-analysis, however, it was found that in women with a history of cervical surgery, cervical length less than 25 mm measured below 24 weeks of gestation was predictive of preterm birth before 35 weeks of gestation. Cervical length measured by transvaginal ultrasound at 24 weeks of gestation was found to be correlated with preterm labor before 37 weeks of gestation, but not with preterm labor before 34 weeks of gestation. In addition, this study showed that a cervical length less than 25 mm may be used as a predictive tool for preterm birth in women who have undergone correction surgery for uterine abnormalities. Last but not least, it was found that the most frequently used gestational age for cervical length ultrasound assessment and prediction of preterm birth is 20–24 weeks [28–32].

In a systematic review study, which included a sample of 1593 women and aimed to assess the accuracy of transvaginally measured cervical length during the second trimester of pregnancy in the prediction of preterm birth in twin pregnancies, it was found that this method of transvaginally measured cervical length works as a better predictor of preterm birth in twin pregnancies than in singleton pregnancies. For this reason, based on the analysis of Honest, women with singleton pregnancies and cervical length at 22–24 weeks of gestation less than or equal to 25 mm exhibited sensitivity and specificity in predicting preterm delivery below 32 and 34 weeks of pregnancy 4.2 and 0.4 and 4.4 and 0.67, respectively, while asymptomatic women with twin pregnancies and cervical length at 20–24 weeks of gestation below 20 mm exhibited sensitivity and specificity in predicting preterm delivery below 32 and 34 weeks of gestation 10.1 and 0.64 and 9.0 and 0.64, respectively [28–32].

Although the present study has, among other things, highlighted the value of transvaginally measured cervical length in the prediction of preterm birth in twin pregnancies, the efficacy of therapeutical practices that are based on the results of such studies and that are aiming to prevent premature birth is not certain. It is critical to note at this point that there is currently no therapeutic method that effectively

seems to prevent premature birth in twin pregnancies, as it has been suggested in singleton pregnancies the implementation of practices such as cervical cerclage and progesterone.

## 4. Cervical cerclage

Cervical cerclage is effective in reducing the risk of preterm birth in high-risk pregnancies. Studies have proven that it contributes to statistically significantly fewer premature births before 33 weeks of gestation.

Specifically, in women with cervical cerclage, the rate of deliveries before 33 weeks was 13% compared to 32% observed in women without cervical cerclage Furthermore, a meta-analysis of randomized trials investigating the effectiveness of ultrasound-guided cervical suture placement in women with a history of second-trimester miscarriage or preterm delivery concluded that deliveries before 35 weeks' gestation were statistically significantly less in cases where suture cervical cerclage was placed compared to cases where some other treatment was followed (RR 0.57; 95% CI 0.33, 0.99 and RR 0.61; 95% CI 0.40, 0.92, respectively). Thus, cervical suture placement as a means of preventing preterm delivery in singleton pregnancies is indicated according to the guidelines in the following cases [32–36]:

History of one or more second-trimester miscarriages associated usually in a future pregnancy with painless cervical dilation and absence of signs of labor or rupture of fetal membranes. History of cervical cerclage in a previous pregnancy due to painless dilatation of the cervix during the second trimester. Painless cervical dilatation was found on physical examination. Ultrasound findings in combination with a history of preterm delivery, i.e. preterm delivery before 34 weeks in a previous pregnancy and cervical length in the current pregnancy below 25 mm as found in an ultrasound check before 24 weeks of pregnancy [36–40].

However, the effectiveness of placing a suture around the cervix of women carrying twins is not entirely certain also, whether the indications for cervical suture placement in twin pregnancies are equivalent to those in singleton pregnancies is still under investigation.

A study comparing selective cervical ligation with simple observation, but without determining whether and what risk factors were present, found no statistically significant difference between the two comparison groups. This result is similar to that of singleton pregnancies where routine cervical cerclage in all pregnancies without appropriate case selection has been found to offer no benefit [36–40].

A meta-analysis of randomized trials involving the use of cervical suture ligation in both singleton and twin pregnancies according to cervical length and setting a threshold of less than 15 mm in singleton pregnancies and less than 25 mm in twin pregnancies concluded that in singleton pregnancies with a positive history, there was a statistically significant benefit in reducing the risk of delivery before 35 weeks (RR 0.74, 95% CI 0.57, 0.96). When there was a miscarriage or premature birth in the second trimester in the history, the probability of risk was even lower (RR 0.57 and 0.61, respectively). However, in twin pregnancies without a positive history, it was seen that cervical ligation increased by 2 times the risk of delivery before 35 weeks of gestation (RR 2.15, 95% CI 1.15, 4.01). This result, however, comes from a single study that included a small number of cases, although it is reasonable to conclude that the placement of a cervical cerclage suture in twin pregnancies in which a short cervical length is found in a random check without the presence of a history, does not offer

a benefit. However, the possible benefit of twin pregnancies with a short cervical length and the presence of risk factors has not yet been clarified.

Furthermore, placing a cervical ligation suture in women with twin pregnancies due to a cervical length of less than 25 mm before 24 weeks gestation and using the sequential cervical length measurement approach found that ligation may clinically significantly reduce preterm birth before 34 weeks compared with conservative management such as bed rest (36.7% in the band group vs. 50% in the rest group) [36–42].

This study demonstrated that suture ligation in twin pregnancies does not harm but instead provides a benefit when cervical length decreases on consecutive ultrasound measurements. Data on the placement of suture cervical cerclage in twin pregnancies with a history of preterm birth or second-trimester miscarriage are unfortunately lacking.

## 5. Cervical cerclage suture placement techniques

Cervical cerclage is defined as the placement of a suture in the cervix to maintain the pregnancy, which can be done through a transvaginal or transabdominal surgical approach. The two transvaginal techniques for ligation are the modified McDonald and the Shirodkar but without finding superiority of one over the other technique. Also, no superiority of one type of non-absorbable suture over another has been found, so the type of suture is freely chosen by the clinician. In the McDonald surgical technique, a simple non-absorbable suture is placed circularly in the cervix at the level of the cervical junction. Retrospective studies have found no benefit in placing a second suture to reinforce or reconstruct the cervical mucosa.

The Shirodkar technique involves the preparation and detachment of the cervical mucosa from the cyst in order to place the suture as close as possible to the height of the internal cervical os. To achieve this, the bladder and rectum are prepared and detached from the cervix, a non-absorbable suture is placed as close as possible to the internal cervical os, and the knot is then covered with mucosa [36–42].

Transabdominal suture placement at the level of the cervical isthmus is preferred in women in whom there is an indication for suture placement but the transvaginal approach is not possible due to anatomical problems (such as after cervical ectomy) or failure of transvaginal suture placement Transabdominal suture placement can be performed either open or laparoscopically depending on the surgeon's clinical experience.

Usually transabdominal banding is done at the end of the first trimester or at the beginning of the second trimester (between 10 weeks and 14 weeks of pregnancy) or before pregnancy and can remain between pregnancies in cases where the delivery is completed by cesarean section [36–42].

## 6. Administration of progesterone: intramuscular administration of progesterone

Intramuscular administration of 17-alpha hydroxyprogesterone is considered to be effective in preventing preterm delivery in singleton pregnancies with a positive history of preterm delivery. Regarding twin pregnancies, intramuscular administration of 17-alpha hydroxyprogesterone 500 mg twice weekly can approximately four-fold reduction in delivery before 32 weeks gestation (RR 3.78,

$p < 0.001$) but cannot reduce the risk of delivery before 37 weeks gestation (RR 1.06, 95% CI 0.75, 1.51) [36–42].

However, no benefit was seen in neonatal-perinatal outcomes when intramuscular progesterone was compared with sham treatment. Thus, at present intramuscular progesterone is not recommended in twin pregnancies, although it would be of particular interest to further clarify its administration in a high-risk group pregnant.

## 7. Vaginal administration of progesterone

Vaginal progesterone appears to reduce the risk of preterm delivery. In a statistical meta-analysis of randomized trials that administered vaginal progesterone to asymptomatic pregnant women with shortened cervical length, vaginal progesterone was found to reduce delivery before 28 weeks of gestation (RR 0.51; 95% CI 0.31, 0.85), before 33 weeks of gestation (RR 0.56; 95% CI 0.31, 0.85) and before 35 weeks of gestation (RR 0.67; 95% CI 0.51, 0.89) [36–42].

Also, the use of vaginal progesterone was associated with a reduction in neonatal mortality and morbidity (RR 0.59; 95% CI 0.38, 0.91). Despite the fact that this tendency was not statistically significant, preterm birth at 33 weeks of gestation was found to be less likely in asymptomatic women with a cervical length of less than 25 mm in the second trimester of pregnancy. Also, the use of vaginal progesterone is associated with a 48% reduction in neonatal mortality as well as in the incidence of neonatal complications (RR 0.52; 95% CI 0.29, 0.93). In twin pregnancies, however, vaginal progesterone has been found not to reduce neonatal mortality and mortality (RR 0.97; 95% CI 0.77, 1.2). It is important to note, however, that in selected cases and with a cervical length below 25 mm before 24 weeks of gestation, vaginal progesterone can significantly reduce neonatal mortality and the incidence of neonatal complications (RR 0.56; 95% CI 0.42, 0.75) [42–46].

The daily recommended dose of progesterone is 90 mg in gel form and 200 mg in vaginal tablets (100 mg twice daily). The efficacy of higher doses of progesterone (400 mg) in reducing preterm birth and neonatal mortality and morbidity has not been proven. There appears to be a trend, but not statistically significant, of an increased incidence of cholestasis of pregnancy in a subgroup of women who received higher doses of progesterone.

## 8. Vaginal pessary

Placement of a ring-shaped plastic around the cervix vaginally has been used to prevent preterm birth for over 50 years, with greater interest being gained since 2003, when it was found that after placement of the pessary in pregnancies there were no preterm births. Thirty-two weeks gestation in a follow-up study of high-risk pregnancies for preterm delivery where a vaginal pessary was placed, delivery before 37 weeks was observed in 50% of women. However, in a randomized study that included singleton pregnancies with a cervical length of 25 mm or less, the rate of preterm delivery in pregnancies who had a pessary inserted was 6%, compared to 27% observed in pregnant women where only follow-up was performed (OR 0.18, 95% CI 0.08, 0.37) [42–46].

In twin pregnancies with a cervical length below the 25th percentile, vaginal pessary use reduced both preterm delivery (before 32 weeks' gestation) and poor

perinatal outcome. Specifically, prematurity was 14% in the vaginal pessary group versus 29% in the monitoring group (RR 0.49, 95% CI 0.24, 0.97), while poor perinatal outcome was 2% in the vaginal pessary group versus 29% in the monitoring group (RR 0.4, 95% CI 0.19, 0.83). The results were even more encouraging in the subanalysis of high-risk pregnancies for the occurrence of preterm birth [42–50].

## 9. Combination of therapeutic approaches

In a systematic review and statistical meta-analysis that included both randomized and non-randomized studies, it was found that only seven studies could be included in the review, which only involved singleton pregnancies, and there was no data on twin pregnancies.

This review found that there was no difference in reducing the risk of preterm delivery before 34 weeks gestation when the combination therapy including vaginal pessary and progesterone was compared with pessary monotherapy (RR 1.3, 95% CI 0.7, 2.42) or administration of progesterone (RR 1.16, 95% CI 0.79, 1.72). In addition, there was no difference in the reduction of preterm birth before 37 weeks gestation when the combined treatment of cervical banding and progesterone administration was compared with cervical banding alone (RR 1.04, 95% CI 0.56, 1.93) or progesterone administration. (RR 0.82, 95% CI 0.57, 1.19) [48, 51–54].

However, as mentioned above, these data are limited and related to singleton pregnancies, while there is no data on twin pregnancies.

Since the 22nd week of gestation and every 2 weeks, there was a steady gradual decrease in the cervical length of the study population. The pattern of this decrease was even present in women who did not eventually give birth before 32 weeks of gestation, and this finding was consistent with existing literature data [48, 51–54]. Ramin observed that this decline became apparent after the 20th week of pregnancy, while Hiersch observed a faster rate of cervical length reduction in triplet pregnancies compared to that noted in twin pregnancies. However, a sharp decrease in cervical length from the 22nd to the 24th week of gestation appeared to be specific to triplet pregnancies that are at increased risk for preterm delivery between 24 and 32 weeks of gestation.

Although in many studies in triplet pregnancies, a short cervix is characterized the one that is less than 25 mm, with a cervical length of 34–35 mm, with sensitivity and specificity of 60–80% and 70–90% respectively, considered as critical in this study. A study conducted by Mheen is one of the few in which the cervical length limit has been set to 30 mm. By applying this limit, however, a predictive accuracy of 87.4% has been achieved. Ideally, this accuracy would reach 100%, something previously attempted through the acceptance of the 20 mm threshold between 25 and 28 weeks of gestation, a limit, though, inconsistent with the findings of the current study. Wherever the "critically short" cervical threshold is set in the various studies, it is advisable to keep in mind that women with shorter cervical lengths may have already been led to miscarriages in the second trimester of pregnancy or to preterm birth and therefore not being included in the sample of the study population. However, all described cervical length limits appear to be relevant in clinical practice, and none of them should be considered more accurate and significant than others [48, 51–54].

Concerning the chorionity of the triplet pregnancies, no significant difference was found in cervical lengths. Thus, chorionity was excluded from the prognostic parameters for preterm birth below 32 weeks of gestation in this study, which is not in the AMPHIA study, and the study of Perdigao and colleagues. Therefore, as far as

the chorionicity in multiple pregnancies is concerned, it is important to deduct more studies with larger numbers of samples to draw safer conclusions [48, 51–54].

The usefulness of measuring the cervical length at different stages of pregnancy has been investigated in addition to doing so during the second trimester of pregnancy using transvaginal ultrasonography. There is a relatively small number of studies evaluating the sensitivity of the cervical length measured before the 16th week of pregnancy in predicting preterm birth, with the results being controversial [54–58].

Studies by Naim, Berghella, and Andrews found a strong association between short cervical length and preterm labor. A study by Hassan found that a "short" cervix at 14–19 weeks is a weaker predictor of preterm birth than an ultrasound assessment of cervical length in mid-pregnancy. Contradictory results were presented by Hasegawa, as well as by Zorzoli, who found in their studies no association between "early" cervical ultrasound assessment and preterm birth [54–58].

Conoscenti in a study with a sample of 2469 women with singleton pregnancies measured cervical length at 13–15 weeks of pregnancy aiming to calculate the risk of preterm birth. It was found that the average gestational age at birth was 40 weeks, with the incidence of preterm birth being 1.7%. In this study, early risk factors, such as previous history of preterm birth, were found to be consistent with those of other studies, and the main finding of this study was the inability to predict women who would eventually be led to premature birth since cervical length was similar to women who gave birth at term compared to the ones who gave birth prematurely, regardless of the presence of risk factors. In other words, the cervical length measured at 14 weeks of gestation appeared in this study, similar between women at high risk of preterm birth and women at low risk [54–58].

This finding is also not in accordance with other studies that show a strong relationship between cervical length's shortening in mid-pregnancy and a history of previous second-trimester miscarriages or preterm births. A possible explanation for this may be the association of a history of previous preterm birth with the risk of preterm birth, a finding presented also by Heath, who recorded apparent cervical lengthening alterations, after mid-pregnancy in the second trimester of pregnancy. A study conducted by Greco, with a sample of 9974 singleton pregnancies and with ultrasonographic cervical length assessment at 11–13 weeks of gestation to assess the risk of preterm birth, found that labor before 34 weeks of gestation, concerning 1% of the study population, could be predicted at 54.8% (95% CI 44.7–64.6) and with false negative rates of 10%, by combining cervical length with various features of the pregnant woman.

A similar study conducted by Sananes, with a sample of 31,834 pregnancies, seemed to detect at 23.3%, with a 10% false negative rate, preterm birth, which accounted for 3.7% of the study population, by ultrasound assessment of cervical length in the first trimester of pregnancy. In another study by Carvalho, cervical length was estimated in the first (11–14 weeks) and second trimester (22–24 weeks) of pregnancy in a random population of singleton pregnancies. The mean cervical length at 11–14 weeks of gestation was found to be 42.4 mm and 38.6 mm at 22–24 weeks of gestation. These findings of the above-mentioned study are consistent with those of other studies. In a study by Zalar, an ultrasound assessment of cervical length in the first trimester of pregnancy (11.3 ± 1.9 weeks) revealed an average cervical length of 46 mm in a low-risk population of pregnant women. In another study by Kushnir, which included 166 low-risk preterm labor women, cervical length was measured at 8–13 weeks of gestation and found to be 43 mm. Moreover, in a study by Guzman, cervical length assessment was performed in 469 high-risk preterm labor

women with continuous ultrasound measurements between 14 and 24 weeks of gestation. Thus, the cervical length was found to be shorter at 21–24 weeks of gestation than at 15–20 weeks of gestation [54–58].

Cervical length during the first trimester of pregnancy, as shown by the above studies, appears to be even longer than that of non-pregnant premenopausal women. This could probably be explained by understanding the role that the lower part of the uterus plays in the cervical segment in the first trimester of pregnancy.

Carvalho observed that cervical length showed a gradual shortening from the first to the second trimester of pregnancy. This decrease in cervical length, however, was more obvious in the group of women who eventually had preterm birth. Cervical length ranged from 42.7 to 39.3 mm in women who gave birth at term, whereas in women who gave birth prematurely, cervical length decreased from 40.6 mm at 11–14 weeks of gestation to 26.7 mm at 22–24 weeks of pregnancy. Given these data, in the group of the women that will have premature birth, the decrease in cervical length occurs between the first and second trimester of pregnancy, and the degree of cervical shortening is related to the degree of prematurity. Guzman has also described this model of cervical shortening, presenting the weekly rate of cervical shortening between 15 and 24 weeks of gestation in women at high risk of preterm birth. To establish the ultrasonographic diagnosis of cervical insufficiency it was necessary in this study to find a progressive decrease in cervical length below 20 mm before 24 weeks gestation. Sufficient cervices showed a non-significant decrease in cervical length (−0.3 mm/week) compared to "insufficient" cervices (−4.1 mm/week, $P < 0.001$). In a study presented by Murakawa, which evaluated the cervical length in 32 women with threatened preterm labor and in 177 normal singleton pregnancies between 18 and 37 weeks of gestation, it was found that cervical length in women with threatened preterm labor was even shorter in women who also had history of preterm birth (23.2 mm compared to 31.7 mm in women with a free history of prematurity) [58–62]. In addition to looking at the significance of cervical length during the first trimester of pregnancy, numerous studies also analyze cervical length during the third trimester of pregnancy to evaluate the risk of preterm birth, but mostly to forecast the time of delivery.

Regarding the correlation of cervical length during the third trimester of pregnancy with preterm delivery, in a study of Papastefanou in 1180 low-risk singleton pregnancies cervical length was measured by ultrasound at 24–30 weeks of gestation. It was found that 0.85% of the study population had preterm birth before 34 weeks of gestation and 5.08% had preterm birth before 37 weeks of gestation. Cervical length in the first group of women who had preterm labor before 34 weeks was shorter (mean 11 mm, $p < 0.001$) than the cervical length of women who gave birth after 34 weeks of gestation (mean cervical length 31 mm). Cervical length was also presented in this study as shorter in the women who had premature birth after 34 but before 37 weeks of gestation (mean cervical length 22 mm, $p < 0.001$) compared to women who eventually gave birth after 37 weeks of gestation (average 31 mm). Thus, it was found that cervical length could predict preterm labor before 34 weeks with a sensitivity of 70% and labor after 34 weeks but below 37 weeks of pregnancy with a sensitivity of 38.3% [34, 54–60]. In another study by Mahmut Kuntay Kokanali, cervical length was measured using transvaginal ultrasound at 34 weeks of gestation in 318 low-risk for preterm birth primiparous women. It was concluded that there was a statistically significant correlation between cervical length at 34 weeks of gestation with the week of gestation that birth took place ($r = 0.614$, $p < 0.001$). After statistical analysis, it was found that cervical length below 25.5 mm predicted preterm labor

over 34 weeks but below 37 weeks with 80% sensitivity, specificity of 93.9%, positive predictive value of 52.6%, and a negative predictive value of 98.2%, while a cervical length above 42.5 mm at 34 weeks of gestation predicted an extension of pregnancy after 41 weeks with 70.4% sensitivity, 93.5% specificity, positive 50% predictive value and 97.1% negative predictive value [58–62]. Regarding the prediction of the successful outcome of labor induction by assessment of cervical length during the third trimester of pregnancy, there are several studies examining this relationship. In one of these studies, Hatfield did not document the use of cervical length as an effective predictor of labor induction success. This review included 20 studies of 3101 women who were about to undergo labor induction and who were subjected to cervical length ultrasonographic assessment before the induction. It was found that cervical length predicted successful labor induction outcome (positive predictive value 1.66, 95% CI 1.20–2.31) as well as failure to induction (negative predictive value 0.51, 95% CI 0.39–0.67) [58–62].

Another systematic review of Saccone's used five 735 singleton pregnancy studies to draw conclusions about the importance of cervical length in predicting the timing of spontaneous birth. It was therefore found that a cervical length of less than 30 mm could predict the automatic start of birth within the following week of the cervical length measurement with 64% sensitivity and 60% specificity. Thus, a woman at term pregnancy and with a cervical length of 30 mm has a less than 50% chance of giving birth within the next 7 days, while a woman with a cervical length of 10 mm has a greater than 85% chance of giving birth within the next 7 days of the measurement. Finally, another systematic review of Verhoeven's used 31 studies of 5029 women to record cervical length and labor outcome. It was found that cervical length predicted cesarean section with sensitivity ranging from 14% to 92% and specificity from 35% to 100%. In particular, cesarean section could be predicted at a cervical length of 20 mm with a sensitivity of 82% and a specificity of 34%, at a cervical length of 30 mm with a sensitivity of 0.64 and a specificity of 0.74%, and at a cervical length of 40 mm with a sensitivity of 13% and specificity of 95% [62–66]. According to the literature, there are many ambiguous and contradictory opinions.

However, in our center, Department of Obstetrics and Gynecology of the Democritus University of Thrace Cervical cerclage is performed at a cervical length shorter than 15 mm. In other cases, at a cervical length greater than 15 mm, pessary is recommended for the pregnant woman. In some cases where, despite the cervix cerclage, a shortening of the cervix is observed, a combination of circumcision and pesso is recommended. In all pregnant women at risk of premature delivery, it is recommended administration of progesterone.

In conclusion, preterm birth continues to complicate 11–12% of all pregnancies with a slightly increasing trend in recent years, which is only partially attributable to the increased number of multiple pregnancies. The impact of preterm birth on public health is very serious as it accounts for 70% of neonatal mortality and 50% of neurodevelopmental problems, and based on the results of this study we conclude that the contribution of transvaginal ultrasound during pregnancy in the early recognition of pregnancies at increased risk for preterm birth is significant.

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