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## Guidelines on prevention of preterm birth

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### ABSTRACT

This guideline has been prepared by the National Maternal Fetal Medicine guidelines committee and approved by the Society of Obstetricians and Gynecologists Pakistan. These recommendations will enable the practicing clinicians to optimally manage pregnancies at risk of preterm birth.

### ARTICLE HISTORY

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Risk factors; preterm birth; screening; prevention

## 1. Introduction

Preterm birth (PTB) refers to delivery that occurs before 37 weeks of gestation [1,2]. It is the single most important determinant of adverse Perinatal and infant outcomes, in terms of survival and quality of life [2]. A vast majority of these children die due to complications of preterm birth [3,4]. and many survivors have lifetime disability. Pakistan is among the 15 countries with a high Perinatal mortality [4]. Therefore Screening for this condition is a priority.

In 70–80% of PTBs are spontaneous and nearly half are born to women with no previous history or are nulliparous [3]. Women with a previous history of Preterm delivery has a 14–15% risk of having a delivery before 35 weeks of gestation compared to 3% if the previous delivery was at term [5,6].

Strategies for prediction of Preterm birth include demographic features and risk factors, sonographic and biochemical markers [1,6]. Following screening, interventions progesterone or cerclage can be offered to women who are classed as high-risk [7].

## 2. Risk factors

Risk factors that are studied include demographic factors, infections and uterine factors. There is no convincing evidence to support its use routinely [8]. However, common risk factors one can look for at the time of first antenatal visit are given in Table 1.

## 2.1. Risk reduction

### 2.1.1. Initial assessment

- Assessment of risk preconception [12].
- Identify risk factors at the time of first antenatal visit.
- Life style modification including cessation of smoking.
- Optimization and control of preexisting medical conditions including hypertension and Diabetes and metabolic syndrome.
- Counseling regarding the risk of PTB in women with twin pregnancy and IVF.

### 2.1.2. Screening for infection

- Screening for asymptomatic bacteriuria.
- Bacterial vaginosis.

## 3. Prediction of PTB by cervical length (CL)

Transvaginal ultrasound for cervical length measurement is the gold standard for prediction of Spontaneous Preterm birth. The risk is inversely related to the cervical length [13–15]. Level of Evidence Grade 11B

When performed by appropriately trained individuals, it is found to be sensitive and highly reproducible [13,14]. Level of evidence Grade 11B. Transvaginal scan for cervical length measurements are unaffected

**Table 1.** Risk factors.

Maternal	Obstetric risks	Uterine factors
Age <18 or above 40years [9].	Previous or family history of Preterm [11]	Uterine malformations [6] Conization of cervix.
High or Low BMI [10] PCOS	Previous history of second trimester abortion	Polyhydramnios
Nulliparous	Lack of antenatal care	Multiple pregnancy [9]
Smoking/Substance abuse [10]	Lack of continuity of care	Infections UTI, bacterial vaginosis [6]
Low socioeconomic status [10]	Vaginal bleeding [6]	IVF pregnancy [6]

by maternal obesity, cervical position, and shadowing from fetal parts [13].

### 3.1. Who should be screened?

- Those with prior history of spontaneous Preterm birth/PPROM [Grade1A]
- Previous history of second trimester miscarriage [13].
- History of uterine anomalies and previous history of surgery of the cervix.
- Cervical length screening can be considered in women from low-risk group. [Grade IIB]. It can only be implemented with adherence to strict guidelines [13] Level of evidence Grade 11A.

### 3.2. Conditions where cervical screening is not indicated : level of evidence grade 11B

- Those with ruptured membranes [13].
- With cerclage in place.

### 3.3. When to perform cervical assessment during pregnancy?

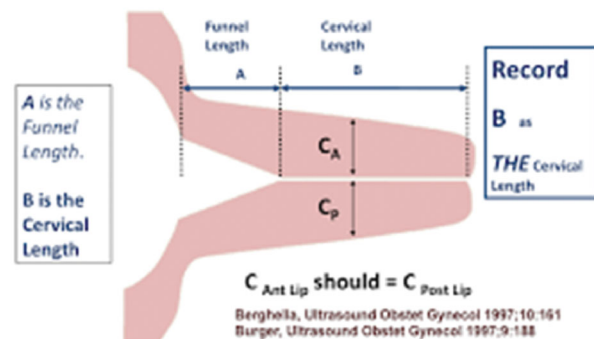
- In low-risk women it is recommended that the examination is performed at the time of anomaly scan.
- In high-risk women there is no consensus on the timing and frequency of cervical assessment [13]. However, cervical length can be performed done at 12–13 weeks and 6 days of pregnancy along with the Nuchal Translucency screening scan and after excluding major anomalies. Level of Evidence 1A.

### 3.4. Criteria for acceptable cervical length measurement

- Bladder should be empty [7].
- Prepare the clean probe by applying a cover.
- Guide the probe to the anterior fornix after introducing it gently.

- Obtain the sagittal long axis view of the entire cervix
- The image of the cervix fills 67–75% of the screen.
- Landmarks to be noted are:
  - ^ Both Internal and external are seen clearly.
  - ^ Cervical length is visible throughout the length.
  - ^ Funneling and debris need to be noted and documented.
- Calipers are placed clearly.
- Examination is performed over a period of time.
- Shortest cervical length is noted of the three good images.
- Fundal and suprapubic pressure is avoided.

### Measurement of the Cervix



Adapted from Berghella V, Ultrasound Obstet Gynecol 1997;10;161 [16].

### 3.5. Frequency of screening in the high-risk women

- Serial cervical assessment is performed every one to two weeks and suture is applied only if cervical length becomes equal to or less than 25 mm [13]. Level of evidence Grade 1.
- Funneling with cervix <25 mm has shown a good predictive value for preterm birth in high-risk women [17]. However, addition of funneling to the cervical length >25 mm does not increase the prediction of PTB [17].

### 3.6. What is the cut off for offering intervention?

- The risk of spontaneous preterm birth is related to the cervical length and depends on a priori risk. A cervical length of <25 mm between 16 and 24 weeks is considered to be short [7].
- Women with cervical length <25 mm tends to deliver significantly earlier compared to those with measurement more than 25mm [8]. In high-risk women cervical length <25 mm between 14 and 18 weeks of gestation has a positive predictive value of 70% compared to 40% at 18–22 weeks of gestation [7].
- Therapeutic interventions can be offered if cervical length is <25mm.

## 4. Interventions

Vaginal progesterone and cerclage are the two interventions proven to be effective in reducing the risk of PTB. RCTs have shown that they reduce the risk of preterm delivery and improve perinatal outcome [18,19].

### 4.1. Progesterone

It is by far the most studied intervention for Preterm birth prevention [19,20]. RCTs have demonstrated significant reduction in PTB with the use of this intervention [19,20].

#### 4.1.1. The use in those with previous history of PTB

Progesterone use in women with previous history resulted in reduced risk of Preterm delivery before 34 weeks of gestation (RR.31) [20]. The perinatal mortality is reduced by half. (RR0.45) [21] Use of vaginal micronized Progesterone reduces the risk of respiratory distress syndrome, neonatal morbidity and admission to NICU [7].

It is given both by intramuscular and Vaginal route [14,15]. In a meta-analysis by Jarde et al. the use of vaginal progesterone significantly reduced preterm birth <33 weeks (OR.29) [22].

#### 4.1.2. Progesterone use with short cervix

A meta-analysis has shown that the use of vaginal micronized progesterone significantly reduces preterm birth <34 weeks of gestation in women with a short cervix. (OR 0.45) In a meta-analysis on individual patient data vaginal progesterone was found to significantly reduce the risk of PTB [18]. Both Neonatal morbidity and mortality are significantly reduced in women using progesterone [19].

### 4.1.3. Use of progesterone in twin pregnancy

Twin or higher order pregnancy with a short cervix will benefit from the use of progesterone. However, its use is not seen to improve the risk of PTB in those with a normal cervix, but it improves the neonatal outcome [22,23].

#### 4.1.4. Recommendations

- Vaginal micronized Progesterone is considered to be safe and effective [21,24].
- It can be used for the prevention of preterm birth in singleton pregnancy with a prior PTB or short cervix. Level of evidence 1A.
- Vaginal micronized progesterone is also recommended in twins with a short cervix. Level of evidence 1A.
- Therapy can be initiated from 16 weeks onwards or any time short cervix is detected. It needs to be continued till 36 weeks of pregnancy. Level of evidence 1A.
- The dose of vaginal progesterone recommended in singleton pregnancy is 200mg daily and those with multifetal gestation is 400mg. The dose is taken preferably in the evening.
- Vaginal Progesterone can be used along with cervical cerclage.

### 4.2. Cervical cerclage

Cerclage is associated with reduction in Preterm birth before 37 weeks in women with prior Preterm birth and short cervix in comparison with no treatment [25]. Wealth of evidence suggests that cerclage reduces the risk of birth before 34 weeks by about 25%. Level of Evidence of Grade II C.

There is no difference in the efficacy of the vaginal progesterone and cerclage in case of a short cervix with previous history of Preterm Birth [26].

If the cervical length is less than 15 mm, cerclage is associated with significant reduction in Preterm birth [27].

Ultrasound indicated cerclage is usually applied from 16 to 22 weeks of Pregnancy. Cerclage can be applied from 12-14 weeks also excluding major anomalies at the time of Nuchal Translucency scan. This is mainly applicable to those with previous history of extreme Premature deliveries, repeated second trimester losses [28] Level of Evidence Grade 1 A.

#### 4.2.1. Recommendations

It is recommended that cerclage is offered to women with:

- If the cervical length in the index pregnancy is less than 25 mm with previous history of Preterm birth. Level of Evidence. 1A.

- In the absence of any history, cerclage for short cervix is not recommended as it carries morbidity. Level of Evidence.
- Cerclage based on previous history alone is not recommended as Cerclage carries morbidity. Level of Evidence 1A.
- In women with previous history of cerclage, cerclage should be offered after performing transvaginal cervical length measurement. Level of Evidence 1VA.
- There is limited data is available on the role of rescue cerclage.
- Current evidence does not support the use of Cervical Pessary does not support the use of cervical pessary for the prevention of Preterm birth. Its use was not found to improve perinatal outcomes in singleton and twin pregnancies with a short cervix. Level of Evidence 1A.

#### 4.2.2. Cerclage in twins and higher order

- Routine use of cerclage for twins is not recommended. Level of Evidence 1VA.
- We recommend Cerclage only after demonstration of short cervix on ultrasound. Level of Evidence 1VA.

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