

## Prediction of Preterm Birth in Women with Short Cervix

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### ABSTRACT

**Background:** Second trimester short cervical length identifies women at increased risk for an early spontaneous Preterm birth (sPTB), hence raising a compelling need for Cervical Assessment for prediction and possible Preventing Preterm Delivery.

**Objective of the study:** to assess the implications associated with a short cervical length as well as the use of ultrasonographic-derived cervical length measurement in predicting preterm birth.

**Methods:** the present review includes relevant randomized controlled trials (RCTs) that investigated the in Medline (via PubMed), Cochrane Library and Embase. Retrospective and Prospective Cohort studies, Case-control and Randomised controlled trials. There were no restrictions by outcomes examined, language or publication status.

**Results:** The critical search results yielded 6 articles (randomized trials=2, cohort studies=3, case-control study=1) representing 653 patients . Five of the 6 presented similar pregnancy outcomes (spontaneous preterm birth or pregnancy loss < 24 weeks' gestation) between the ultrasound-indicated and the history-indicated cerclage groups. 45–69% of the patients followed with cervical ultrasound were able to avoid cerclage.

**Conclusion:** Evidence from randomized trials supports that transvaginal ultrasound is predictive of preterm birth in women with prior preterm birth and a short cervix. The thresholds proposed vary from 15 mm to 28 mm and cerclage is thus recommended.

**Keywords:** Preterm birth, labour, ultrasound, cerclage, incompetent cervix, transvaginal, transperineal, cervical length, pPROM., obstetric ultrasound; prediction.

### INTRODUCTION

Preterm birth, defined as childbirth occurring at less than 37 completed weeks or 259 days of gestation<sup>1</sup>. In almost all high- and middle-income countries of the world, preterm birth is the leading cause of child death<sup>2</sup>. Being born preterm also increases a baby's risk of dying due to other causes, especially from neonatal infections<sup>3</sup>.

Preterm birth estimated to be a risk factor in at least 50% of all neonatal deaths<sup>4</sup>. Children who are born prematurely have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term.

The morbidity associated with preterm birth often extends to later life, resulting in enormous physical, psychological and economic costs<sup>5</sup>. Estimates indicate that in 2005 the costs to the United States of America alone in terms of medical and educational expenditure and lost

productivity associated with preterm birth were more than US\$ 26.2 billion<sup>6</sup>.

Worth mentioning that 28% of all the early neonatal deaths all (deaths within the first 7 days of life) that are not interrelated to congenital malformations, are due to preterm birth<sup>7</sup>. Preterm birth rates have been reported to range from 5% to 7% of live births in some developed countries, but are estimated to be substantially higher in developing countries<sup>8</sup>. These figures appeared to be on the rise<sup>9</sup>. Events leading to preterm birth are still not completely understood, although the etiology is thought to be multifactorial. It is, however, unclear whether preterm birth results from the interaction of several pathways or the independent effect of each pathway. Causal factors linked to preterm birth include medical conditions of the mother or fetus, genetic influences, environmental exposure, infertility

treatments, behavioural and socioeconomic factors and iatrogenic prematurity<sup>9</sup>.

Preterm birth is a syndrome with a variety of causes which can be classified into two broad subtypes: (1) spontaneous preterm birth (spontaneous onset of labour or following prelabour premature rupture of membranes (pPROM)) and (2) provider-initiated preterm birth (defined as induction of labor or elective caesarean birth before 37 completed weeks of gestation for maternal or fetal indications (both "urgent" or "discretionary"), or other non-medical reasons<sup>10</sup>.

Most PTBs are spontaneous, arising from the onset of labor or from preterm premature rupture of membranes. Prediction and prevention of spontaneous preterm birth continue challenging priorities for obstetricians worldwide<sup>11</sup>. It has been hypothesized that spontaneous preterm birth can be caused by several etiologies resulting in a final common pathway of shortening the cervix as the terminal event prior to preterm delivery or preterm prelabour rupture of membranes (PPROM)<sup>12</sup>. Numerous studies have clearly demonstrated that the relationship between a sonographic short cervix and spontaneous preterm birth is most sensitive when combining cervical length and obstetric history in high-risk populations with previous preterm birth<sup>13</sup>. A cut-off value of cervical length of 25 mm has been used by clinicians and researchers to screen for women at the highest risk of spontaneous preterm birth<sup>14</sup>. Recently, this group of women has been targeted with interventions to reduce the risk of spontaneous preterm birth including vaginal progesterone, cerclage and cervical pessary<sup>15</sup>. In addition, current practice guidelines recommend initiation of therapy in high-risk patients with a cervical length of < 25 mm in the midtrimester<sup>16</sup>.

Nevertheless, the risks for women with a previous spontaneous preterm birth with a normal cervix in pregnancy may not be negligible.

Building on the fact that the risk of preterm birth was inversely correlated to the length of the cervix as measured by ultrasound which was an observation confirmed in multiple studies using different techniques, the most widely acknowledged and used technique is transvaginal ultrasound<sup>17</sup>.

A number of interventions based on this observation have been studied in randomized trials. A recent meta-analysis<sup>18</sup> has looked at its efficacy in preventing preterm birth. Since the publication of the 2001 SOGC guideline<sup>19</sup>, there have been numerous studies on imaging, natural history, and use of transvaginal ultrasound in common clinical scenarios, as well as a number of randomized trials looking at interventions for a short cervix. This updated guideline provides a comprehensive review of studies of shortened cervical length diagnosed on transvaginal ultrasound and is broader in scope than the 2001 guideline<sup>19</sup>.

Various sonographic findings have been described, including cervical length shortening (with multiple different cutoffs suggested), the presence of a funnel, and dynamic changes either spontaneously or with provocative measures. These findings have been utilized to select women for treatment, generally cerclage.

In the present review, we aim to assess interventions associated with a short cervical length as well as the use of ultrasonographic-derived cervical length measurement in predicting preterm birth.

## **MATERIALS AND METHODS**

### **Data Sources**

Published literature was retrieved through searches of PubMed and The Cochrane Library and Embase up to December 2016, using appropriate controlled vocabulary and key words.

### **Study Selection and Criteria**

**Search results were screened by scanning abstracts for the following:**

**Search terms:** Preterm birth, labour, ultrasound, cervix, incompetent cervix, transvaginal, transperineal, cervical length, fibronectin.

### **Inclusion Criteria:**

- 1- Retrospective and prospective cohort studies, Randomized controlled trials (RCTs) and observational studies.
- 2- Studies conducted on women who had one or more early spontaneous preterm births less than 34 weeks' gestation.
- 3- No language restriction.

### **Exclusion Criteria:**

Duplicated studies, studies with irrelevant outcome and endpoints which is the prediction of PTB in Women with short cervical length

and the implication of the ultrasound-induced cerclage.

**RESULTS**

In this systematic review, pregnancy outcomes and cerclage-related complications of ultrasound-indicated versus history-indicated cerclage in patients with suspected cervical insufficiency were compared. ultrasound-indicated cerclage was compared to history-indicated cerclage in women with a singleton gestation.

After screening for eligibility in terms of relevance and quality, 6 articles <sup>20-25</sup> were selected and

included, RCTs=2, cohort studies=3, case-control study=1. Five <sup>20,22,23,24,25</sup> of which revealed similar pregnancy outcomes (spontaneous preterm birth or pregnancy loss < 24 weeks' gestation) between the ultrasound-indicated and the history-indicated cerclage groups. Nonetheless, in one <sup>21</sup>prospective cohort study preterm birth was significantly lower in the ultrasound-indicated group. (Table 1).

**Table 1:** Description of 6 Studies included in the Systematic Review

| # | Author                   | Year | Study Design         | N   | Inclusion Criteria   | Prior mid-trimester birth                          | Criteria for U/S-indicated cerclage  | Underwent U/S-indicated cerclage |
|---|--------------------------|------|----------------------|-----|--|--|--|----------------------------------|
| 1 | Beigi <sup>20</sup>      | 2005 | RCT                  | 97  | Singleton pregnancies, history of spontaneous PTD (15–32 weeks) or mid-trimester loss with painless and progressive dilation of the cervix | 43%  | CL ≤ 20 mm at < 24 weeks' gestation  | 54%                              |
| 2 | Higgins <sup>21</sup>    | 2004 | Prospective Cohort   | 135 | Prior spontaneous PTD (20–36 weeks) or mid-trimester loss, previous forced dilation, cone biopsy   | 53%  | CL < 25 mm at ≤ 24 weeks' gestation  | 32%                              |
| 3 | Groom <sup>22</sup>      | 2004 | Case-control         | 81  | History of spontaneous PTB or mid-trimester loss, history of cervical surgery  | Mean 1.2 in cerclage group versus 1.08 in Controls | CL ≤ 15 mm, or progressive shortening to ≤ 25 mm, funneling of at least 50% before the 3 <sup>rd</sup> trimester | 36%                              |
| 4 | Berghella <sup>23</sup>  | 2002 | Retrospective Cohort | 177 | Singletons, prior spontaneous PTD or mid-trimester loss, risk factors for cervical insufficiency   | 46%  | CL < 25 mm, funneling at least 25%, before 24 weeks' gestation   | 36%                              |
| 5 | To <sup>24</sup>         | 2002 | Retrospective Cohort | 90  | Singletons, prior spontaneous PTD (16–33 weeks) or mid-trimester loss  | 27%  | CL ≤ 25 mm before 24 weeks' gestation  | 60%                              |
| 6 | Althuisius <sup>25</sup> | 2000 | RCT                  | 73  | Singletons, spontaneous PTD 15–34 weeks with painless dilatation or PPROM not preceded   | Mean 1.2 in cerclage group versus 0.8 in           | CL ≤ 25 mm at < 27 weeks' gestation  | 23%                              |

|  |  |  |  |  |                         |  |  |
|--|--|--|--|--|-------------------------|--|--|
|  |  |  |  | by contractions,<br>“suspected cervical<br>incompetence” | Observation<br>al Group |  |  |
|--|--|--|--|--|-------------------------|--|--|

It is of significant importance to note that 45–69% of the patients followed with cervical ultrasound were able to evade cerclage. It can be concluded that despite the fact that using ultrasound shortened cervical length to select women with suspected cervical insufficiency for cerclage reduces cerclage rates, it also yields pregnancy outcomes similar to cases where cerclage was placed on the basis of clinical suspicion alone. Based on this systematic review, women with suspected, yet non-classic cervical insufficiency may undergo mid-trimester transvaginal cervical length assessment to optimize the needed surgical candidate intervention.

## DISCUSSION

The old model of viewing the cervix as competent or incompetent has been replaced with the new concept of the cervix functioning along a biologic continuum of reproductive performance and premature cervical ripening, similarly, from one or a combination of multiple interrelated factors and biologic pathways. The interpretation of current clinical data underlines that ultrasound screening and treatment regimens should be limited to a highly selected population of women with a prior spontaneous preterm birth and may also be applicable to patients with suspected, but non-classic histories of cervical insufficiency. Women with a prior spontaneous preterm birth represent a population that can clearly benefit from transvaginal ultrasound measurement of cervical length<sup>23,26</sup> the recently completed trial<sup>26</sup> emphasizes the inclusion of women with prior early spontaneous preterm birth < 34 weeks. Currently, only women with a preterm birth history should be considered for such routine sonographic screening and cerclage placement. Nevertheless, the findings from this trial<sup>26</sup> are not completely prescriptive regarding the optimal cervical length cutoff for ultrasound-indicated cerclage; however in planned secondary analyses, improved obstetric outcomes were demonstrated using the trial’s entry cervical length cutoff of 25 mm, recognizing that the beneficial effect is significantly more pronounced in women with very short cervical length less than 15 mm.

### Limitation of the study

One of the profound limitations to the present review was that the 6 articles reports evaluated

heterogeneous populations. In addition to that and although the incidence of prior mid-trimester loss was appreciable, the majority of the studies provided insufficient data to draw firm conclusions regarding cerclage-related complications for comparison.

## CONCLUSION

Ultrasonographic cervical measurement as a diagnostic tool is a safe and effective technique to predict increased risk of preterm delivery in particular women. The transvaginal route seems to be the most well studied and is satisfactory to women; nevertheless, the transperineal route can also be used if the patient declines the transvaginal route. It can also be used to prevent unnecessary interventions in women at increased risk of preterm delivery if the result is reassuring. In contrast, routine prenatal transvaginal ultrasound screening of cervical length in low-risk populations is not supported by available evidence.

Evidence from randomized trials supports the recommendation of cerclage in patients with a prior preterm birth and a short cervix. The thresholds suggested vary from 15 mm to 28 mm. Further evidence is also needed with respect to the utility of measuring fetal fibronectin in combination with measurements of cervical length.

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