

# Relationship between cervical dilation and time to delivery in women with preterm labor

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**Background:** Early recognition of the signs and symptoms of preterm labor (PTL) is important in order to establish treatment. Our aim was to determine the relation between cervical dilation and time interval from admission to delivery in women with preterm labor. **Materials and Methods:** A retrospective cohort study was conducted on 83 singleton gestations admitted for preterm labor between 24 weeks and 34 weeks, who subsequently delivered preterm. Women were categorized into three groups of cervical dilation (0-2 cm, 3-6 cm, >6 cm) and the time interval from admission to delivery was compared. Cox regression analysis was performed to assess the association between cervical dilation and time interval from admission to delivery. The other variables examined were gestational age (GA) at admission and length of the cervix, when performed. **Results:** The time interval from admission to delivery was significantly shorter in women with higher dilatation of the cervix ( $p < 0.02$ ) and in those admitted at a more advanced gestational age ( $p < 0.05$ ). Forty-eight percent of women with cervical dilatation 0-2 cm delivered in the first 48 h compared to 85% of the women with a dilatation of 3-6 cm. No significant association was found between the length of the cervix and the time interval to delivery. **Conclusion:** Dilatation of the cervix and gestational age at admission are associated with the time interval to delivery in women with preterm labor. The assessment of the length of the cervix is unlikely to add clinical information in women with an already dilated cervix.

**Key words:** Length of cervix, gestational age, obstetric labor, premature birth, uterine cervix dilatation

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## INTRODUCTION

Preterm delivery (PTD), defined as birth before 37 weeks of gestational age, occurs with an incidence of 5-11% and is the leading cause of perinatal mortality and morbidity in developed countries.<sup>[1,2]</sup> Preterm delivery presents a complex etiopathogenesis, which consists of multiple pathological signalings and activation of one or more components of the common pathway of parturition.<sup>[3]</sup> One of the clinical conditions that often precedes spontaneous preterm delivery is threatened preterm labor (PTL), defined as the presence, between 24 weeks and 34 weeks, of the following symptoms: at least eight contractions per hour or four contractions in 20 min and documented cervical changes with intact membranes.<sup>[4]</sup> If spontaneous preterm birth can be predicted, effective therapeutic strategies can be used to improve neonatal outcomes.

Although over the years, many studies investigated the mechanisms involved in the cascade of preterm delivery and the methods for the prevention and early diagnosis of PTL, few studies have been performed on cervical dilation.<sup>[5-9]</sup> How *et al.*<sup>[5]</sup> found that dilatation of the cervix in women with threatened PTL was inversely associated with time from admission to delivery. In another study, the same inverse relation was shown for women with PTL treated with tocolytic agents.<sup>[6]</sup> Early recognition of the signs and symptoms of PTL is important in order to establish a tocolytic therapy and to allow antenatal steroids. Dilatation of the cervix is one of the parameters to be evaluated for the diagnosis of threatened PTL, and it may have an important role in the risk stratification of women presenting with PTL. On the basis of these considerations, the aim of this study was to evaluate the relation between dilatation of the cervix and time between threatened PTL and subsequent preterm delivery.

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## MATERIALS AND METHODS

This was a retrospective cohort study on patients admitted to the Department of Maternal and Child Health of Careggi University Hospital in Florence, Tuscany, Italy between 2010 and 2013, who delivered before 37 weeks. This hospital is a tertiary care center with approximately 3,500 deliveries per year. The local ethics committee approved this study.

Patients with singleton gestations presenting with spontaneous PTL between 24 weeks and 34 weeks and who delivered before 37 weeks were included. During the study period, 83 women who met the inclusion criteria were identified.

Preterm labor was defined as the presence of at least eight contractions per hour or four in 20 min and documented cervical changes with intact membranes.<sup>[4]</sup> Women with multiple gestations, premature rupture of membranes, and those who delivered preterm due to iatrogenic intervention for reasons other than active labor were excluded from the analysis. In addition, women admitted for threatened PTL who were then discharged from the hospital were excluded from the analysis as they represented cases of “false” PTL. Data were collected from the electronic medical records maintained by the Department of Maternal and Child Health. Data included demographics, medical and obstetric history, dilatation and effacement of the cervix at the time of admission, length of the cervix when available, treatment received, and delivery information. The length of cervix was measured by the physician using the appropriate technique.<sup>[10]</sup> This consists of the insertion of a clean transvaginal probe covered by a condom in the anterior fornix of the vagina after the woman has emptied her bladder. When a sagittal long-axis view of the entire endocervical canal is obtained, the image is enlarged until the cervix occupies at least two-thirds of the screen and both the external and internal os are seen. The length of the cervix is then measured from the internal to the external os along the endocervical canal, avoiding excessive pressure on the cervix. After obtaining three measurements, the shortest measurement in millimeters is recorded.

Gestational age estimation was based on the last menstrual period or on the ultrasound performed during the first trimester of pregnancy, when the discrepancy between the two dates was more than 7 days. At our institution, tocolytic therapy is usually administered when necessary only after 24 weeks and until 34 weeks, and it is associated with the administration of betamethasone for fetal lung maturity. Tocolysis is usually used for  $\leq 48$  h to allow betamethasone to act fully. Atosiban is our first-choice drug.

## Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20 (SPSS Inc., Chicago, IL, USA). Normality of continuous data was tested using the Shapiro-Wilk test. Women were categorized into three groups of cervical dilatation (0-2 cm, 3-6 cm, >6 cm). We first evaluated the time interval between admission and delivery in relation to dilatation of the cervix at admission. Cox regression analysis was performed to assess the association between cervical dilatation at admission and prolongation of pregnancy. Time interval from admission to delivery was used as a response in survival analysis; spontaneous delivery was the event. Curves were censored at 7 days. Other variables examined for their association with time interval to delivery were gestational age at admission (<28 weeks, 28-32 weeks, and >32 weeks) and length of the cervix (<2 cm or  $\geq 2$  cm). We also assessed the association between dilatation of the cervix at presentation and the risk of spontaneous preterm delivery at less than 32 weeks, using a Mann-Whitney *U* test. Chi-square test was used to compare categorical variables. A *p* value <0.05 was considered to be statistically significant.

## RESULTS

During the study period, 83 women who met the inclusion criteria were identified. Maternal demographic and obstetric characteristics are reported in Table 1. The median gestational age at admission was 29 weeks and at delivery was 30 weeks. The median interval between admission and delivery was 2 days. When the dilatation was less than 3 cm ( $n = 65$ ), 23% of the women delivered in the first 24 h, 25% between 24 h and 48 h while 52% delivered after 48 h. When the dilatation was 3-6 cm ( $n = 14$ ), 64% of the women delivered in the first 24 h, 21% between 24 h and 48 h, and the remaining 15% after 48 h. An interval of more than 7 days between admission and delivery was observed

**Table 1: Maternal demographic and obstetric characteristics**

Characteristic	Value
Maternal age (y)	31 $\pm$ 6.3
Caucasian race (%)	64 (77)
Nulliparity (%)	43 (52)
Previous preterm birth (24-36 weeks)* (%)	11 (13)
Smoking <sup>†</sup> (%)	8 (10)
Alcohol or drug abuse (%)	1 (1.2)
Gestational age at admission (weeks)	29 (25, 32)
Cervical dilatation at admission (cm)	1 (0, 2)
Cervical effacement >50% at admission (%)	77 (93)
Cervical length at admission (mm) <sup>‡</sup>	14 (6, 22)
Tocolytic therapy (%)	57 (69)
Interval between admission and delivery (days)	2 (0, 6)
Gestational age at delivery (weeks)	30 (26, 33)

Data are presented as *n*(%), mean  $\pm$  standard deviation or medians (25<sup>th</sup>-75<sup>th</sup> percentiles), \*Missing data for three women, <sup>†</sup>Missing data for two women, <sup>‡</sup>Data available for 56 women

in 25% of the women with dilatation of the cervix less than 3 cm and only in 7% of the women with cervical dilation between 3 cm and 6 cm. Only four patients had a dilatation greater than 6 cm at presentation, and they delivered in the first 24 h.

Cox regression analysis showed a significant difference in the time interval from admission to delivery between the three groups of dilatation [ $p < 0.02$ ; Figure 1a]. The higher the dilatation, the shorter was the time interval from admission to delivery. Cox regression analysis also showed that a lower gestational age at admission was significantly associated with a longer time interval to delivery [ $p < 0.05$ , Figure 1b]. Data on the length of the cervix were available for 56 women, who had a cervical dilatation  $< 3$  cm. No significant association was found between the length of the cervix at admission and time from admission to delivery [ $p = 0.69$ , Figure 1c].

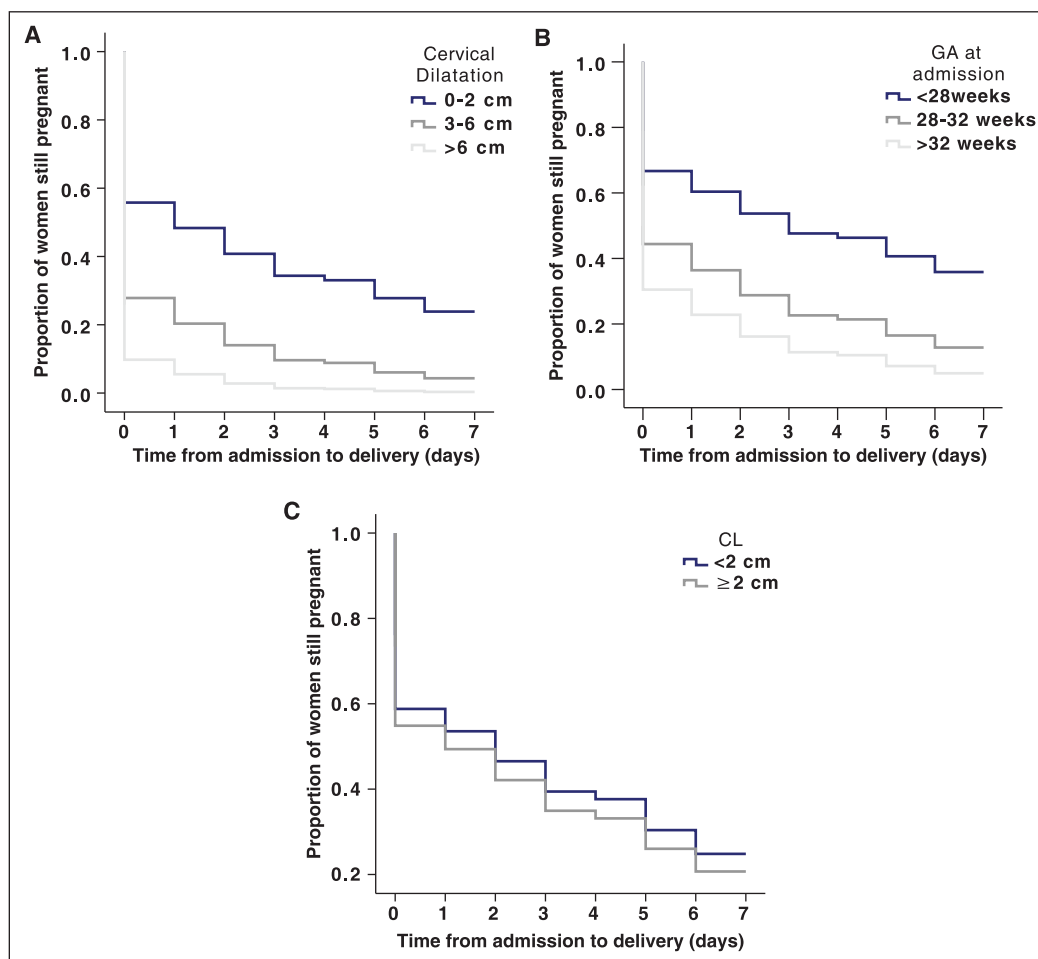
Women with a dilatation of the cervix between 0 cm and 2 cm had a median interval of 3 days between admission and delivery [interquartile range (IQR) 1-7.5] while women with

a dilatation between 3 cm and 6 cm had a median interval of less than 1 day (IQR: 0-1.3); the difference was statistically significant ( $p = 0.01$ ). Fifty-seven women (69%) received a tocolytic therapy. Tocolytic therapy was performed more frequently in women with  $< 4$  cm dilatation of the cervix. The median interval between admission and delivery in women who received tocolytic therapy was 2 days (IQR: 0-8.5) while in those who did not receive treatment, it was 0.5 days (IQR: 0-6) but the difference was not statistically significant ( $p = 0.10$ ).

When considering women presenting with PTL before 32 weeks ( $n = 62$ ), univariate analysis showed that a more advanced dilatation and an earlier gestational age at admission were associated with a higher risk of delivering before 32 weeks ( $p = 0.002$ ). After logistic regression analysis, dilatation of the cervix and gestational age at presentation remained independent predictors of delivery  $< 32$  weeks ( $p = 0.01$ ).

## DISCUSSION

Dilatation of the cervix is one of the parameters that are systematically evaluated in women presenting with PTL.



**Figure 1:** Displays the pattern of time interval from admission to delivery of subjects with different cervical dilations (a), gestational ages (b) and cervical lengths (c). Curves are censored at 7 days. GA = Gestational age, CL = Cervical length

We aimed to evaluate the relation between dilatation of the cervix and pregnancy prolongation in women with PTL and subsequent preterm delivery. Our results showed that the time interval from admission to delivery was associated with dilatation of the cervix and gestational age at admission. These findings are in agreement with the results of previous studies.<sup>[5-7]</sup>

In our population, the median interval between admission and delivery was significantly higher (3 days) for women with dilatation of the cervix between 0 cm and 2 cm compared to women with a dilatation of 3-6 cm (less than 24 h). This time interval is of particular importance in view of the administration of antenatal steroids for pulmonary maturation in women with threatened PTL. Our results support the recommendation of some authors to limit tocolytic treatment to women with maximal cervical dilatation  $\leq 5$  cm,<sup>[11]</sup> because of the lower success rate in the presence of more advanced dilatation. However, data on tocolysis and advanced preterm labor are limited and the appropriate management is controversial.<sup>[12-14]</sup>

In our study, 48% of women presenting with 0-2 cm dilatation of the cervix delivered in the first 48 h, while 85% of women with a 3-6 cm dilatation delivered in the same time period. These percentages are higher than those reported in some previous studies<sup>[5-7]</sup> and indicate that a dilatation of 3-6 cm increases by two times the risk of delivery in the first 48 h compared to a lower dilatation. The high percentage of women delivering in the first 48 h is probably related to the fact that all women in our study had advanced preterm labor, thus constituting a group at a very high risk of delivering prematurely. Amon *et al.*<sup>[7]</sup> reported a high percentage of women with cervical dilatation of 3 cm or more for whom delivery was delayed by 24 h (75%) or 48 h (60%). Similarly, Guinn *et al.*<sup>[6]</sup> found that at 4 cm, 52% of the women remained undelivered at 48 h. All women enrolled in these studies received tocolytic therapy. In contrast to these studies, we selected women who were admitted to our Department and who subsequently delivered before 37 weeks during the same hospital admission, while we excluded women admitted for threatened PTL who were then discharged from the hospital and were considered cases of "false" PTL. Similar to our results on women with dilation 3-6 cm, a recent retrospective study reported that up to 60% of women presenting with advanced cervical dilatation prior to 34 weeks' gestation gave birth within 24 h.<sup>[15]</sup>

Our results also show that for women presenting at a gestational age  $< 32$  weeks, a more advanced dilatation of the cervix and an earlier gestational age at presentation are independent predictors of delivery  $< 32$  weeks, and these findings are in accordance with a previous study.<sup>[5]</sup>

Our study brings the attention on one aspect of PTL that often played only a marginal role in the prediction of preterm birth since it represents a late finding. Currently, the assessment of the length of the cervix alone or in combination with fetal fibronectin is used in clinical practice to predict preterm delivery.<sup>[16]</sup> Ultrasound measurement of cervical length is in fact the most accurate method.<sup>[10,17]</sup> We found no correlation between the length of the cervix at admission and time interval to delivery. This finding suggests that in women with an already dilated cervix, the ultrasound examination of the cervix for the prediction of PTD is unlikely to add information of clinical value, as confirmed by one previous study.<sup>[18]</sup> Other studies report a significant correlation between the length of the cervix and the time interval to delivery, in women with cervical dilatation  $< 3$  cm.<sup>[19,20]</sup> The results of our analysis on the length of the cervix may be limited by the small number of women for whom the measurement was performed (67% of cases).

The correct identification of women at risk for giving birth prematurely after diagnosis of PTL would help to improve maternal and neonatal outcomes. In fact, estimating the risk of imminent delivery is important in order to determine the need for hospitalization, tocolytic therapy and steroids, or to consider maternal transfer to a high-risk center if delivery is not imminent. Our data provide new information for the counseling and obstetric management of women presenting with PTL. A dilatation of 3 to 6 cm doubles the risk of delivering in the next 48 h compared to a dilatation of 0 to 2 cm. Fifty-two percent of women who had preterm labor with cervical dilatation 0-2 cm can have delivery delayed by at least 48 h.

The main limitation of this study lays in its retrospective design. Therefore, some data that were not collected at time of admission are missing, such as the results of the fetal fibronectin (fFN) test, available in only a small number of patients. Among the numerous biomarkers studied in relation to PTD, fFN showed the best results, given its high negative predictive value (99%).<sup>[16,21]</sup> However, cervicovaginal fFN test is most accurate in predicting spontaneous PTD within 7-10 days of testing among women with symptoms of threatened PTL before advanced cervical dilatation.<sup>[16,22]</sup> For this reason, for most women in our cohort the test was not performed. Another limitation was that cervical length was available in only a small number of patients. Finally, quantitative measurement of strength of uterine contractions was not available, since such measurement is not routinely performed at our center.

## CONCLUSION

Dilatation of the cervix and gestational age at admission are significantly associated with the interval between admission and delivery. The measurement of cervical length is unlikely

to add information of clinical value in women with an already dilated cervix. Although dilatation of the cervix is an independent predictor of the time of delivery in women with preterm labor, its predictive accuracy as a single measurement is relatively limited. Further studies evaluating the combination of digital examination with other predictors, such as fetal fibronectin test, are necessary in order to increase our ability to predict preterm delivery.

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#### Conflicts of interest

Authors report no conflict of interests.

#### AUTHOR'S CONTRIBUTION

MDT contributed in the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. VS contributed in the conception of the work, drafting and revising the draft, analysis and interpretation of data for the work approval of the final version of the manuscript, and agreed for all aspects of the work. FV contributed in the conception of the work, conducting the study, revising the draft, acquisition of data for the work approval of the final version of the manuscript, and agreed for all aspects of the work. MC contributed in the conception of the work, revising the draft, acquisition of data for the work, approval of the final version of the manuscript, and agreed for all aspects of the work. MS contributed in the conception of the work, conducting the study, revising the draft, acquisition of data for the work, approval of the final version of the manuscript, and agreed for all aspects of the work. TS contributed in the conception of the work, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

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